

## SUPPLEMENTARY MATERIALS

### Multidimensional chemobehavior analysis of flavonoids and neuroactive compounds in zebrafish

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**Supplementary Materials.** Summary data and statistics for all tested compounds and chemical inhibition studies, including time-course, binned and normalized concentration response curves, mean  $\pm$  SD for normalized activity with 95% confidence intervals, N-values and p-values (two-way repeated measures ANOVA with Tukey's post-hoc,  $p \leq 0.05$ ). Naïve 120 hpf larval zebrafish were exposed (static non-renewal) to multiple concentrations of each chemical individually for 5 hours and locomotor activity was measured immediately following application of treatment. Locomotor activity was binned into 30 min time-bins and normalized to the respective time-bin control group (0.1% DMSO). All excluded treatment groups due to precipitation or acute lethality are noted.

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# Neuroactive drugs and toxicants

## **14 tested chemicals:**

Bumetanide

Caffeine

Chlorpyrifos

Dopamine Hydrochloride

Epinephrine

Fluoxetine

Imidacloprid

S-(+)-Ketamine

Mecamylamine

(+)-Methamphetamine

Methyllycaconitine

(-)-Nicotine

N-methyl-D-aspartic acid (NMDA)

Tricaine mesylate (MS-222)

**CHEMICAL: Bumetanide**

**Normalized percent activity**

**Time bin (minutes post exposure)**

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 81	100 $\pm$ 75	100 $\pm$ 85	100 $\pm$ 74	100 $\pm$ 77	100 $\pm$ 75	100 $\pm$ 80	100 $\pm$ 76	100 $\pm$ 58	100 $\pm$ 70	15
1	81 $\pm$ 47	66 $\pm$ 43	63 $\pm$ 49	68 $\pm$ 57	60 $\pm$ 43	64 $\pm$ 48	61 $\pm$ 46	68 $\pm$ 51	65 $\pm$ 37	74 $\pm$ 45	15
10	74 $\pm$ 75	63 $\pm$ 47	88 $\pm$ 67	116 $\pm$ 103	77 $\pm$ 62	75 $\pm$ 65	100 $\pm$ 90	98 $\pm$ 69	79 $\pm$ 55	94 $\pm$ 58	16
100	84 $\pm$ 59	63 $\pm$ 40	63 $\pm$ 33	83 $\pm$ 43	80 $\pm$ 46	63 $\pm$ 37	75 $\pm$ 40	78 $\pm$ 42	68 $\pm$ 35	67 $\pm$ 43	16
1000	121 $\pm$ 80	128 $\pm$ 149	104 $\pm$ 115	112 $\pm$ 100	96 $\pm$ 82	88 $\pm$ 70	80 $\pm$ 76	81 $\pm$ 61	80 $\pm$ 68	115 $\pm$ 113	16

**Mean  $\pm$  standard deviation**

**Normalized percent activity**

**Time bin (minutes post exposure)**

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	58-142	61-139	56-144	62-138	60-140	61-139	59-141	61-139	70-130	64-136
1	56-105	44-88	38-88	39-97	37-82	39-89	37-85	42-94	46-84	51-97
10	36-111	39-86	54-121	65-168	46-108	43-108	55-145	63-132	51-106	65-123
100	54-113	43-84	46-80	62-105	57-103	44-81	55-95	57-99	50-85	45-88
1000	81-160	53-202	46-161	62-162	55-136	53-123	42-118	50-111	46-114	59-172

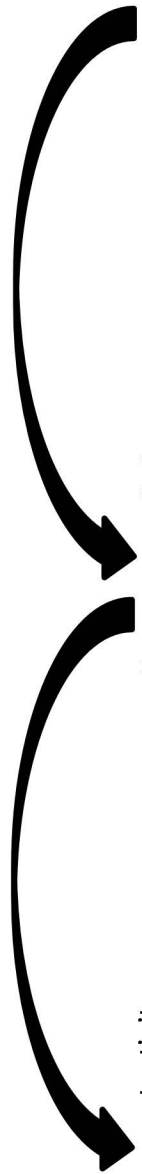
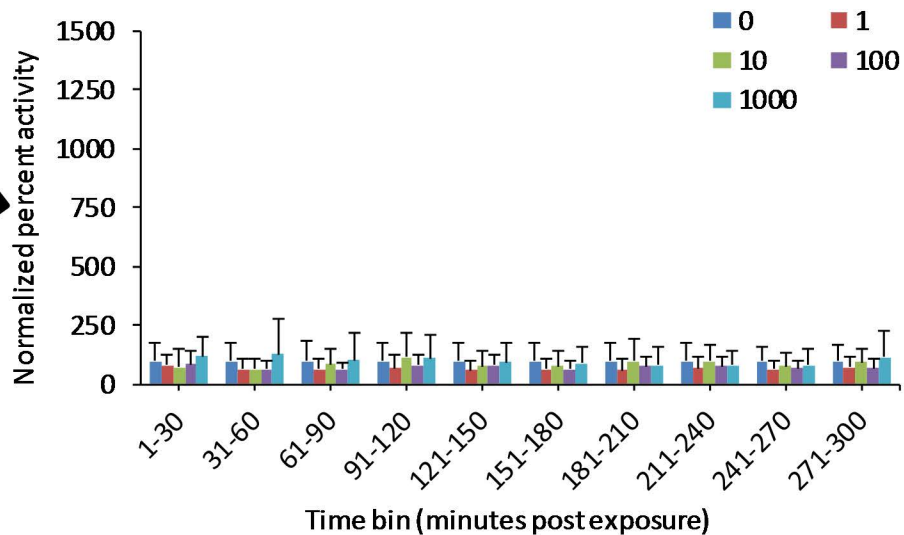
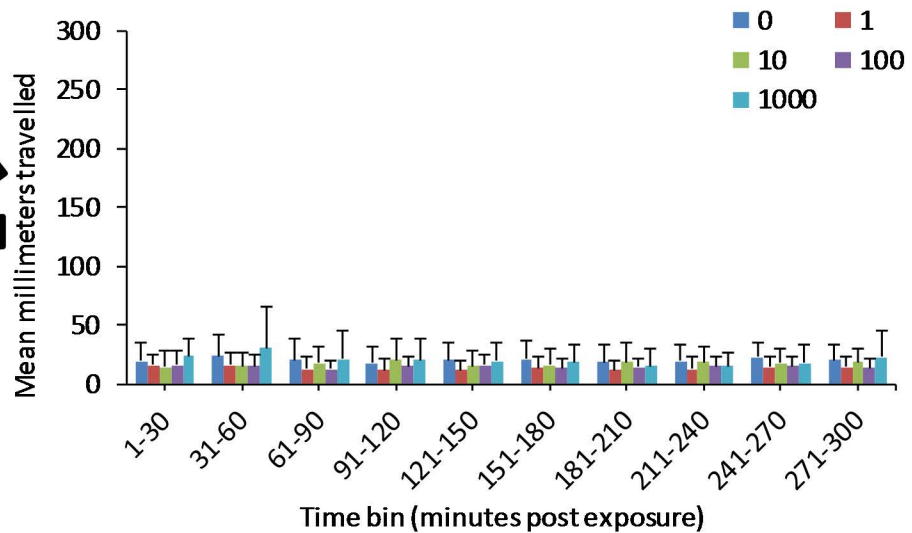
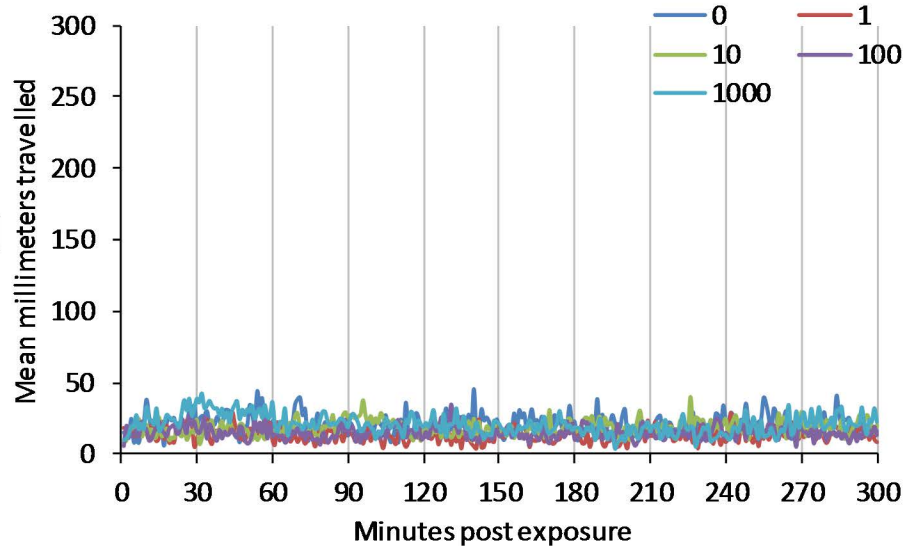
**95% confidence interval**

**p-values**

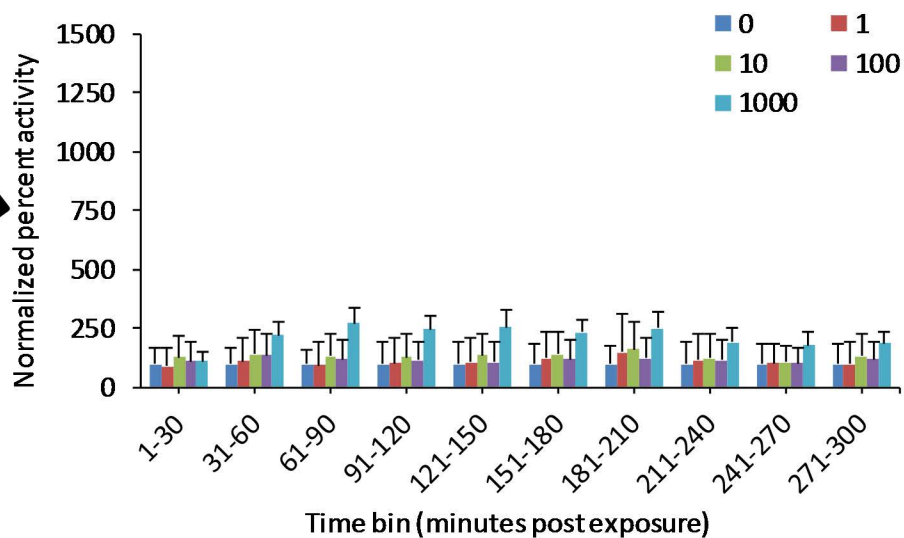
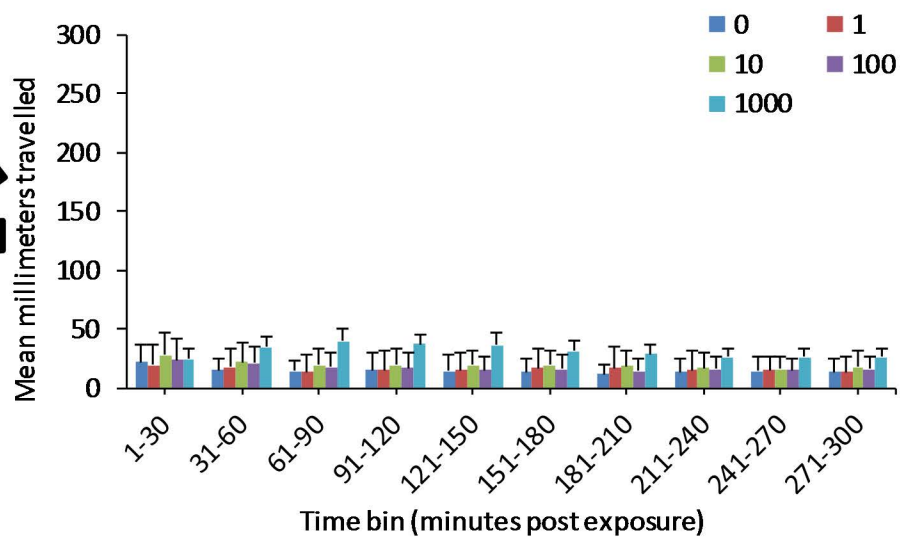
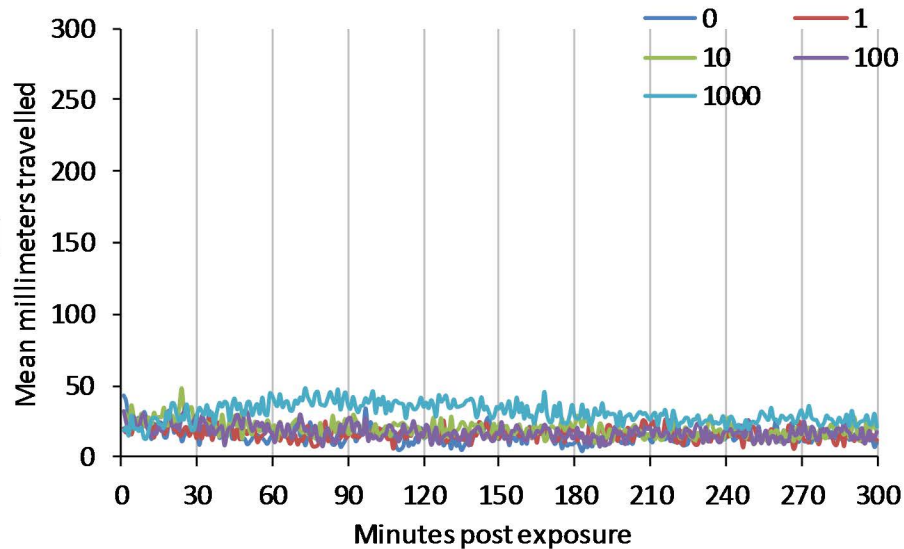
**Time bin (minutes post exposure)**

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.996	0.802	0.807	0.740	0.611	0.618	0.792	0.875	0.770	0.892
10	0.833	0.716	1.000	0.996	0.909	0.678	1.000	1.000	0.841	1.000
100	0.999	0.750	0.965	1.000	0.998	0.685	0.998	0.997	0.878	0.749
1000	0.864	0.997	1.000	0.990	0.998	0.981	0.909	0.989	0.900	0.999

**Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$**



# CHEMICAL: Caffeine



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 67	100 ± 64	100 ± 61	100 ± 96	100 ± 93	100 ± 81	100 ± 75	100 ± 90	100 ± 86	100 ± 85	23
1	90 ± 82	113 ± 101	95 ± 100	104 ± 108	108 ± 102	122 ± 118	147 ± 162	116 ± 115	102 ± 84	98 ± 98	23
10	129 ± 89	139 ± 106	131 ± 92	130 ± 97	134 ± 94	140 ± 96	160 ± 115	125 ± 101	107 ± 73	132 ± 99	24
100	109 ± 85	135 ± 93	119 ± 86	115 ± 81	105 ± 86	118 ± 89	125 ± 85	117 ± 85	101 ± 67	118 ± 76	24
1000	112 ± 43	219 ± 63	271 ± 69	246 ± 61	253 ± 77	233 ± 58	250 ± 68	193 ± 60	177 ± 55	188 ± 52	22

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	72-128	73-127	74-126	60-140	61-139	66-134	69-131	62-138	64-136	64-136
1	55-124	71-155	53-137	59-148	66-151	72-171	80-215	68-164	67-137	57-139
10	93-165	96-182	93-169	90-170	96-173	101-179	113-207	84-166	77-137	91-172
100	74-144	97-173	84-154	82-149	70-140	81-154	91-160	83-152	74-129	87-149
1000	94-130	192-246	242-300	219-272	220-286	208-258	221-279	167-219	154-201	166-210

## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.777	1.000	0.929	1.000	0.998	0.997	0.924	0.998	1.000	0.999
10	0.773	0.818	0.900	0.753	0.520	0.544	0.397	0.895	0.983	0.773
100	0.998	0.703	0.987	0.881	0.994	0.965	0.914	0.931	0.987	0.843
1000	0.802	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.005	0.002

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Chlorpyrifos

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 77	100 $\pm$ 85	100 $\pm$ 84	100 $\pm$ 78	100 $\pm$ 75	100 $\pm$ 65	100 $\pm$ 81	100 $\pm$ 80	100 $\pm$ 79	100 $\pm$ 67	21
1	81 $\pm$ 53	117 $\pm$ 68	137 $\pm$ 88	169 $\pm$ 96	146 $\pm$ 66	166 $\pm$ 73	144 $\pm$ 75	128 $\pm$ 60	147 $\pm$ 65	165 $\pm$ 56	21
10	422 $\pm$ 98	845 $\pm$ 181	1067 $\pm$ 354	911 $\pm$ 400	710 $\pm$ 351	591 $\pm$ 388	316 $\pm$ 243	233 $\pm$ 176	240 $\pm$ 214	239 $\pm$ 243	18
100	323 $\pm$ 72	433 $\pm$ 142	344 $\pm$ 190	148 $\pm$ 143	91 $\pm$ 86	72 $\pm$ 98	47 $\pm$ 79	28 $\pm$ 50	16 $\pm$ 37	12 $\pm$ 27	19

## Mean $\pm$ standard deviation

<sup>‡</sup>Exclusion: lethality observed in 1000  $\mu$ M treatment group (20 of 20 animals)

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	66-134	63-137	63-137	66-134	67-133	72-128	65-135	65-135	66-134	71-129
1	58-105	87-147	99-176	127-211	117-174	134-198	112-177	102-164	119-175	140-189
10	376-468	759-930	900-1233	722-1099	544-875	408-774	202-431	150-316	139-341	124-353
100	290-356	367-498	257-431	83-214	52-131	27-117	11-84	5-51	-1-33	-1-24

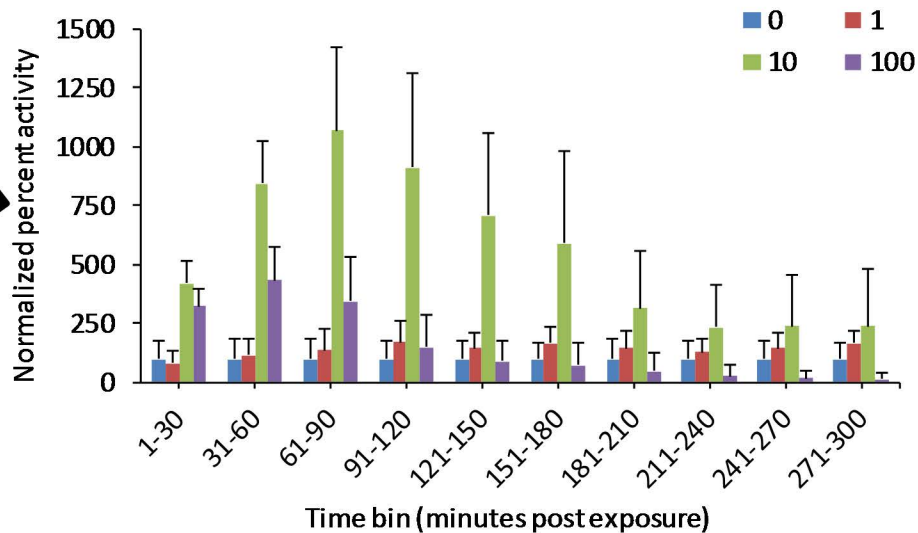
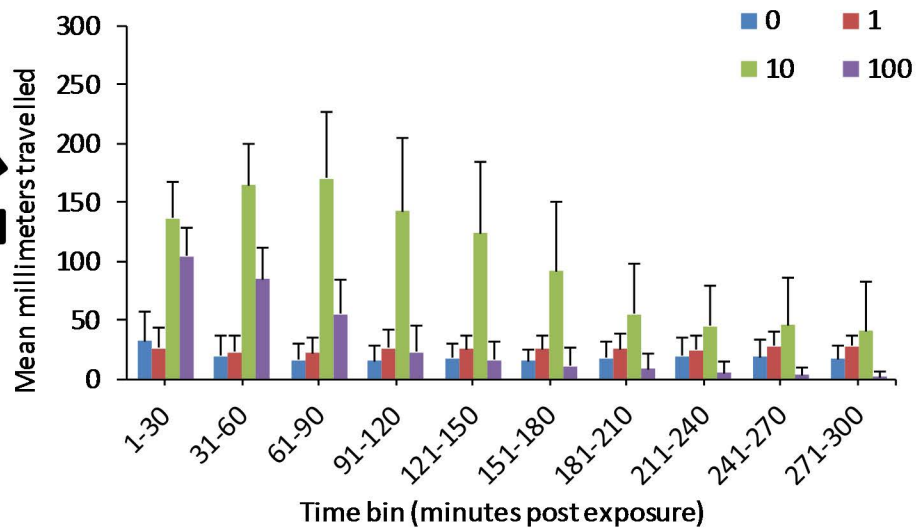
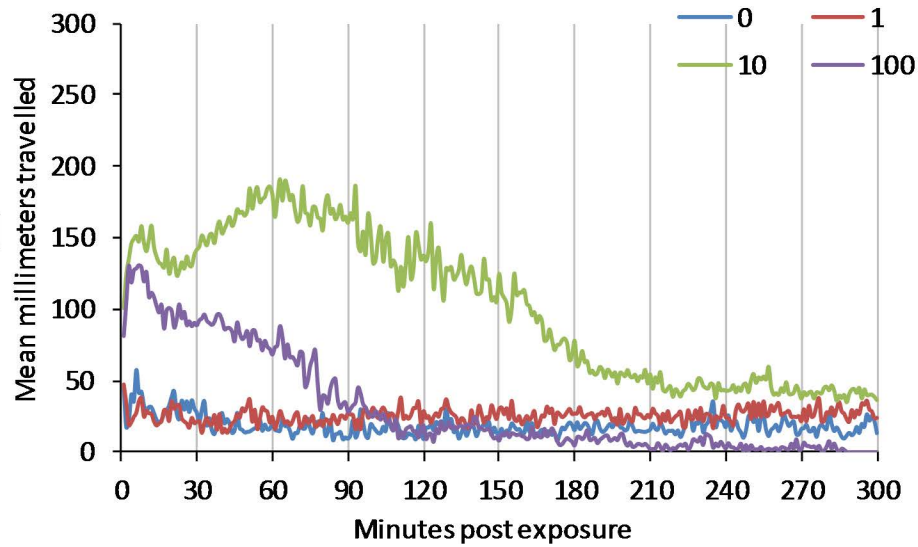
## 95% confidence interval

## p-values

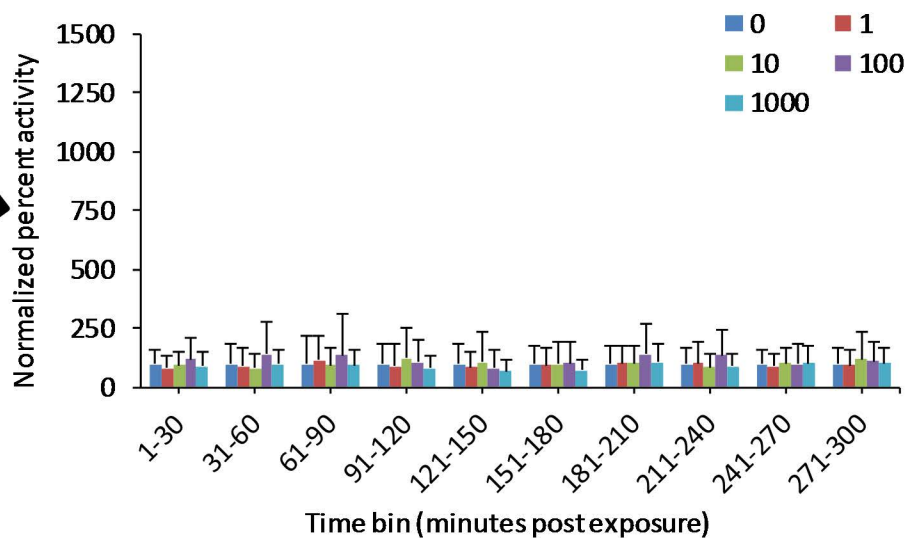
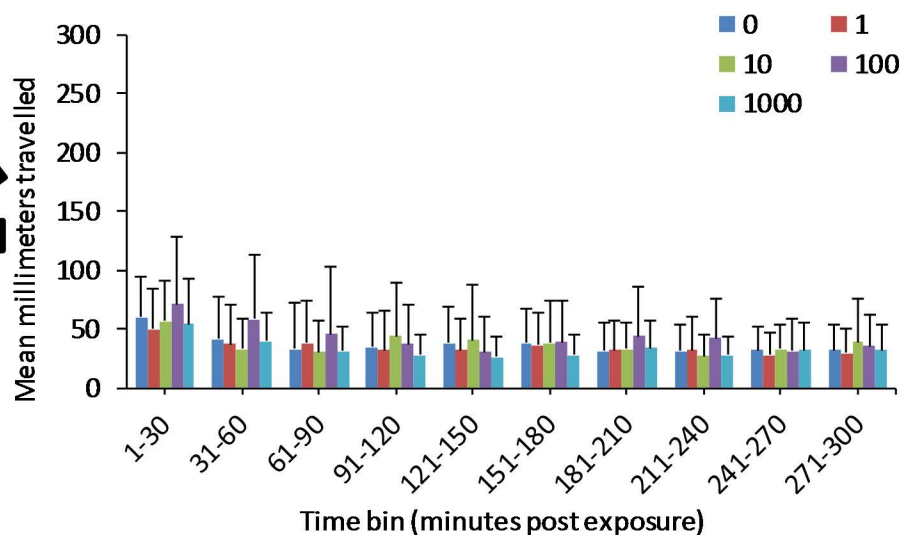
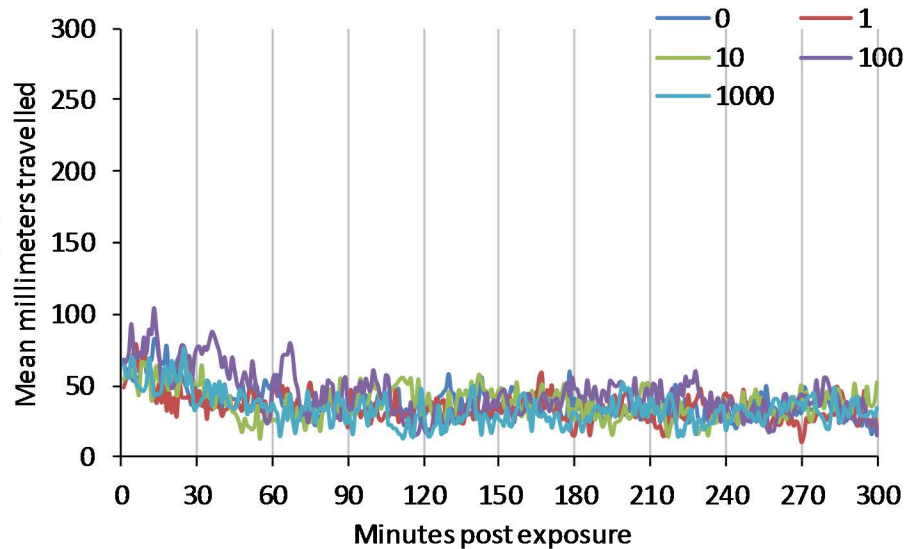
## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.785	0.815	0.513	0.207	0.339	0.184	0.351	0.556	0.178	0.117
10	0.001	0.001	0.001	0.001	0.001	0.001	0.013	0.232	0.372	0.780
100	0.001	0.001	0.001	0.954	0.417	0.023	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Dopamine



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 58	100 ± 88	100 ± 119	100 ± 84	100 ± 81	100 ± 74	100 ± 75	100 ± 72	100 ± 60	100 ± 65	24
1	83 ± 55	90 ± 81	114 ± 108	91 ± 96	84 ± 70	94 ± 72	102 ± 79	102 ± 93	88 ± 57	93 ± 64	21
10	94 ± 57	80 ± 62	92 ± 78	125 ± 128	107 ± 125	100 ± 93	104 ± 73	87 ± 56	103 ± 63	121 ± 114	24
100	117 ± 96	142 ± 132	138 ± 173	107 ± 93	79 ± 81	101 ± 93	140 ± 132	135 ± 109	98 ± 89	110 ± 86	20
1000	90 ± 63	97 ± 59	93 ± 63	79 ± 52	69 ± 47	74 ± 46	108 ± 74	88 ± 52	102 ± 73	101 ± 68	22

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	76-124	64-136	51-149	66-134	67-133	70-130	70-130	70-130	75-125	74-126
1	59-107	55-125	66-161	49-133	53-114	63-126	68-136	61-142	63-113	65-121
10	71-118	55-105	61-124	72-177	55-158	62-138	74-134	64-110	77-129	74-167
100	74-161	83-201	61-25	65-148	43-115	60-143	81-199	86-184	58-137	71-148
1000	63-117	71-122	66-120	57-101	49-89	54-94	76-140	66-110	71-133	73-130

## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.892	1.000	0.949	0.965	0.924	0.956	0.999	0.992	0.953	0.997
10	0.991	0.990	1.000	0.995	0.968	0.994	0.999	0.957	1.000	0.972
100	0.998	0.645	0.729	1.000	0.777	1.000	0.785	0.883	0.971	0.999
1000	0.891	0.981	0.995	0.980	0.658	0.663	0.999	0.972	0.997	1.000

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Epinephrine

**Normalized percent activity**

	Time bin (minutes post exposure)										
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 105	100 $\pm$ 94	100 $\pm$ 92	100 $\pm$ 69	100 $\pm$ 84	100 $\pm$ 111	100 $\pm$ 70	100 $\pm$ 64	100 $\pm$ 54	100 $\pm$ 47	21
1	100 $\pm$ 93	100 $\pm$ 102	113 $\pm$ 132	114 $\pm$ 107	82 $\pm$ 78	103 $\pm$ 63	75 $\pm$ 41	102 $\pm$ 66	88 $\pm$ 52	95 $\pm$ 60	24
10	127 $\pm$ 86	145 $\pm$ 113	126 $\pm$ 140	85 $\pm$ 75	97 $\pm$ 86	111 $\pm$ 80	82 $\pm$ 56	115 $\pm$ 72	94 $\pm$ 71	93 $\pm$ 68	23
100	86 $\pm$ 59	96 $\pm$ 60	118 $\pm$ 81	117 $\pm$ 80	107 $\pm$ 55	128 $\pm$ 68	102 $\pm$ 52	132 $\pm$ 78	132 $\pm$ 82	133 $\pm$ 76	23
1000	98 $\pm$ 73	83 $\pm$ 77	93 $\pm$ 81	91 $\pm$ 86	76 $\pm$ 71	95 $\pm$ 66	62 $\pm$ 42	100 $\pm$ 65	89 $\pm$ 77	110 $\pm$ 98	23

Mean  $\pm$  standard deviation

**Normalized percent activity**

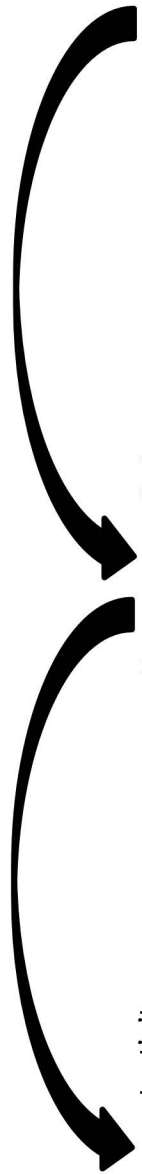
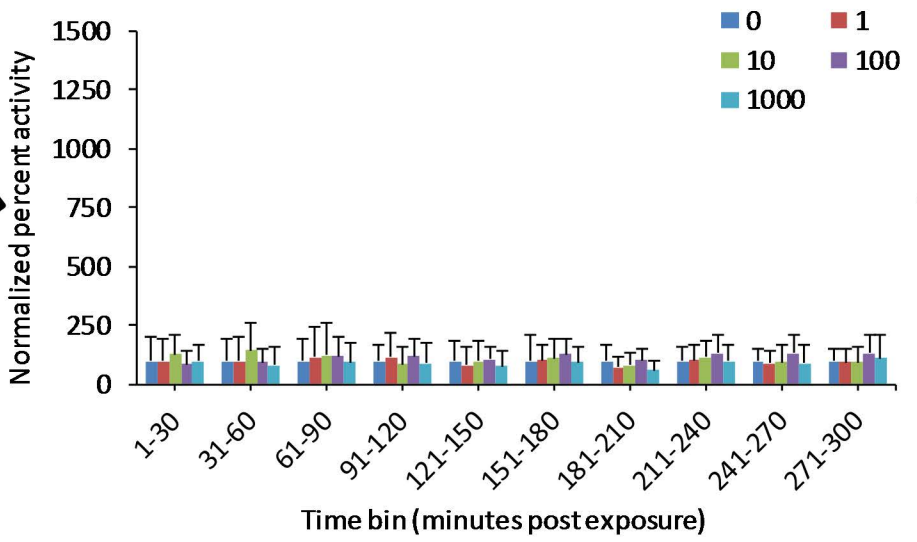
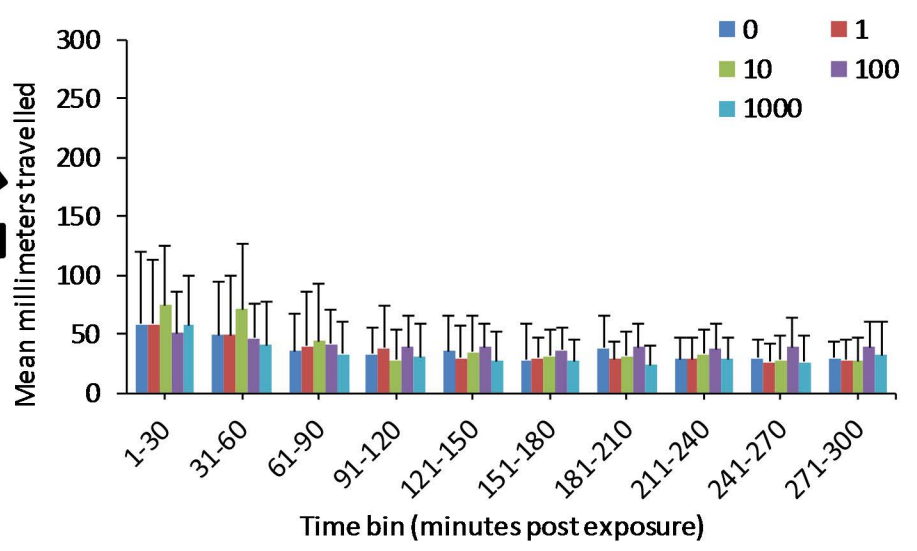
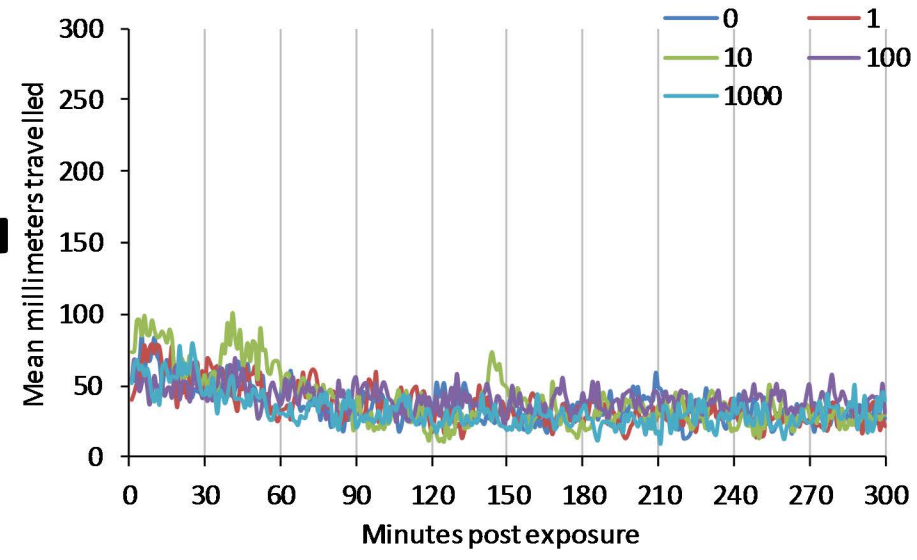
	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	54-146	59-141	60-140	70-130	63-137	52-148	69-131	72-128	76-124	79-121
1	62-138	58-142	59-167	71-158	50-114	78-129	58-92	75-129	67-109	70-119
10	91-163	98-192	67-184	54-116	61-133	78-145	58-105	85-145	65-124	65-121
100	61-111	71-120	84-152	84-151	85-130	100-156	80-123	99-164	98-167	101-164
1000	67-128	51-115	59-127	55-127	46-105	68-123	44-79	73-128	57-122	69-151

95% confidence interval

**p-values**

	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.983	1.000	1.000	1.000	0.873	0.916	0.900	1.000	0.972	0.977
10	0.369	0.853	1.000	0.795	0.989	0.977	0.825	0.985	0.905	0.940
100	0.997	0.985	0.888	0.983	0.936	0.411	0.997	0.733	0.848	0.902
1000	0.980	0.860	1.000	0.918	0.818	0.996	0.288	1.000	0.850	0.987

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$





# CHEMICAL: Fluoxetine

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 107	100 $\pm$ 127	100 $\pm$ 108	100 $\pm$ 16	100 $\pm$ 89	100 $\pm$ 87	100 $\pm$ 83	100 $\pm$ 85	100 $\pm$ 71	100 $\pm$ 124	16
1	16 $\pm$ 25	14 $\pm$ 19	10 $\pm$ 15	13 $\pm$ 20	13 $\pm$ 19	19 $\pm$ 43	27 $\pm$ 50	41 $\pm$ 102	15 $\pm$ 22	11 $\pm$ 28	16
10	21 $\pm$ 38	21 $\pm$ 27	10 $\pm$ 10	17 $\pm$ 33	25 $\pm$ 40	81 $\pm$ 100	204 $\pm$ 145	251 $\pm$ 213	219 $\pm$ 172	197 $\pm$ 153	16

## Mean $\pm$ standard deviation

<sup>‡</sup>Exclusion: lethality observed in 100  $\mu$ M treatment group (16 of 16 animals)

<sup>‡</sup>Exclusion: lethality observed in 1000  $\mu$ M treatment group (16 of 16 animals)

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	47-153	36-164	46-154	42-158	55-145	56-144	59-141	57-143	65-135	38-162
1	4-29	4-23	2-17	3-23	4-23	-2-41	2-52	-10-92	4-26	-3-25
10	2-39	8-35	5-15	1-34	5-45	31-131	132-277	144-357	133-305	121-274

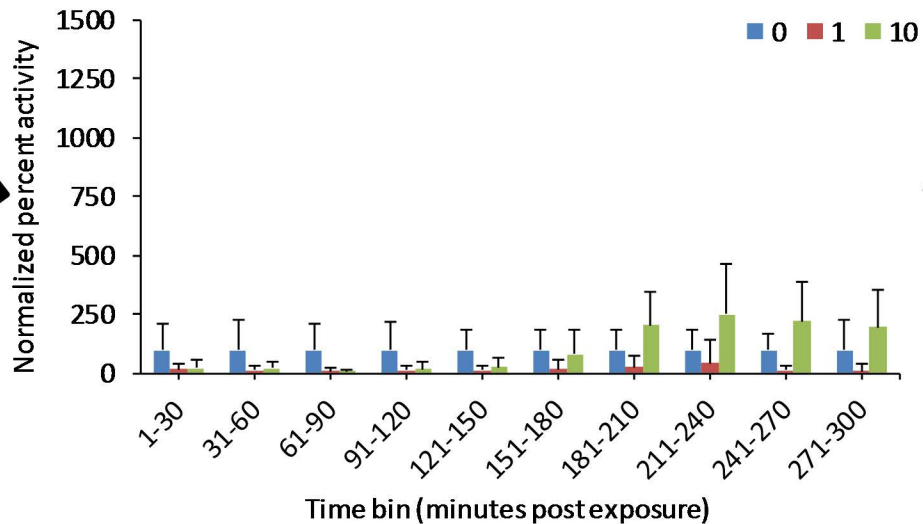
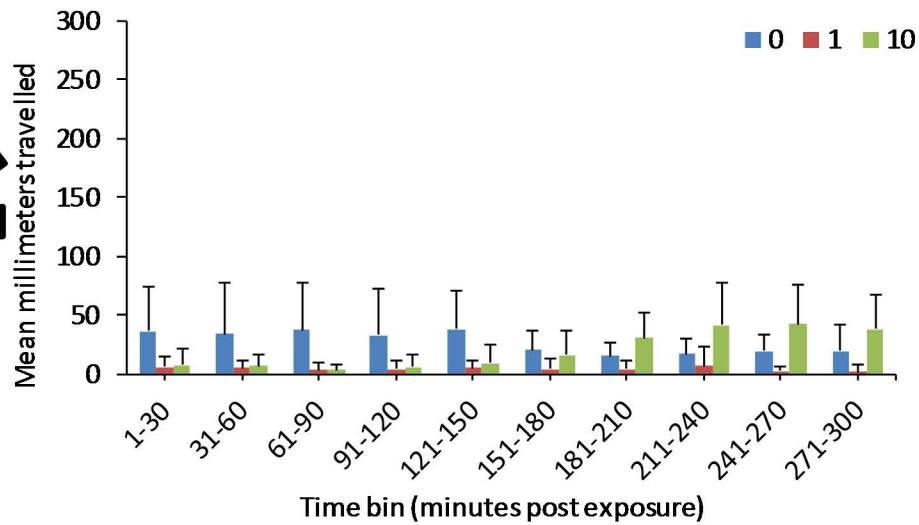
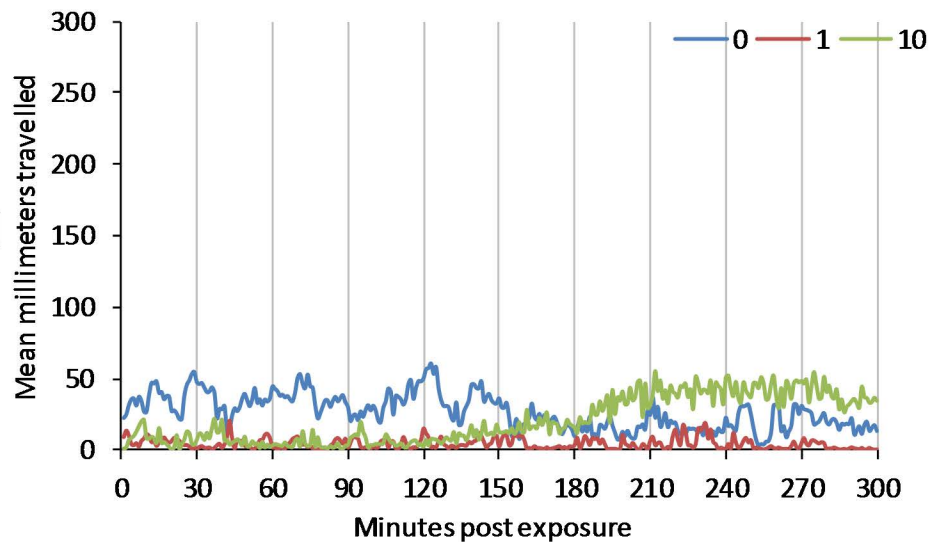
## 95% confidence interval

## p-values

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.002	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001
10	0.001	0.015	0.001	0.002	0.006	0.368	0.232	0.250	0.199	0.107

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Imidacloprid

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 75	100 $\pm$ 116	100 $\pm$ 112	100 $\pm$ 88	100 $\pm$ 101	100 $\pm$ 84	100 $\pm$ 83	100 $\pm$ 100	100 $\pm$ 100	100 $\pm$ 128	16
1	242 $\pm$ 229	287 $\pm$ 341	145 $\pm$ 125	154 $\pm$ 147	123 $\pm$ 148	127 $\pm$ 101	170 $\pm$ 224	101 $\pm$ 68	131 $\pm$ 154	118 $\pm$ 121	16
10	266 $\pm$ 177	159 $\pm$ 113	129 $\pm$ 139	149 $\pm$ 146	149 $\pm$ 174	157 $\pm$ 134	116 $\pm$ 112	112 $\pm$ 96	139 $\pm$ 132	125 $\pm$ 107	16
100	217 $\pm$ 228	156 $\pm$ 130	46 $\pm$ 51	90 $\pm$ 99	86 $\pm$ 149	85 $\pm$ 86	101 $\pm$ 171	47 $\pm$ 44	81 $\pm$ 81	87 $\pm$ 112	16
1000	142 $\pm$ 145	96 $\pm$ 113	23 $\pm$ 32	50 $\pm$ 48	61 $\pm$ 79	40 $\pm$ 46	59 $\pm$ 60	49 $\pm$ 37	38 $\pm$ 37	51 $\pm$ 57	16

## Mean $\pm$ standard deviation

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	63-137	42-158	44-156	56-144	50-150	58-142	59-141	50-150	50-150	36-164
1	128-357	117-458	82-207	80-228	49-197	77-178	58-282	67-135	54-207	58-179
10	178-355	102-215	59-198	76-222	62-236	90-223	60-172	64-160	73-205	72-179
100	103-331	91-221	20-72	40-139	12-161	41-128	16-187	25-69	40-121	31-143
1000	69-214	39-152	7-38	26-74	22-101	17-63	29-89	30-68	20-57	23-80

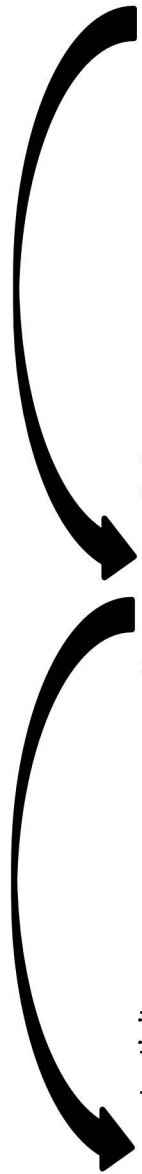
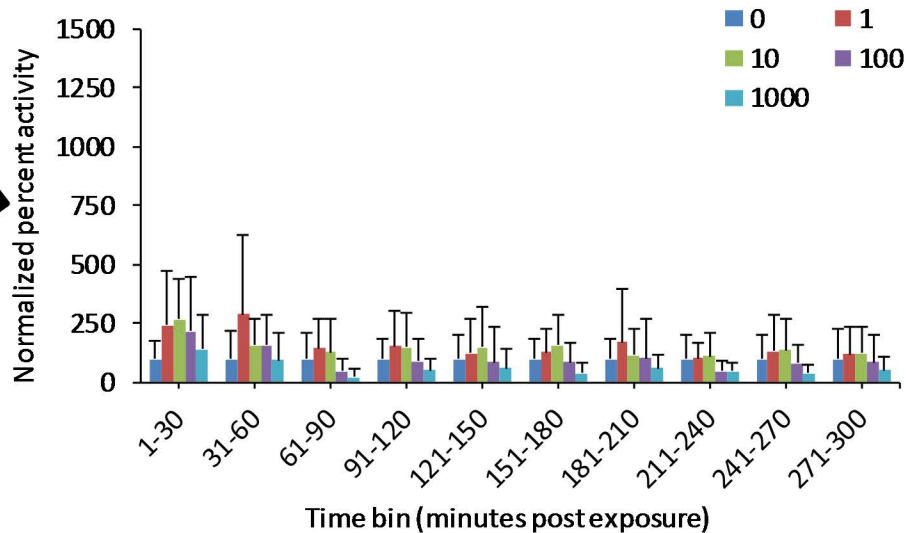
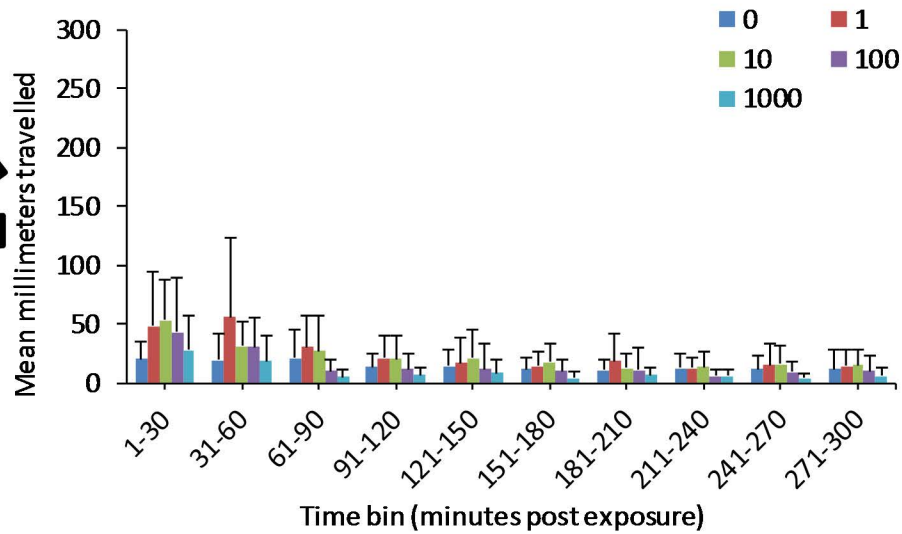
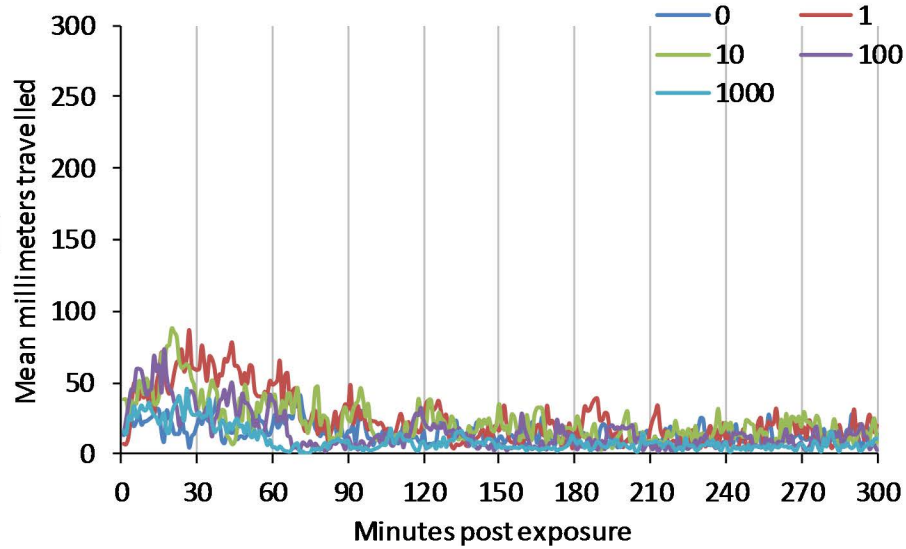
## 95% confidence interval

## p-values

## Time bin (minutes post exposure)

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.220	0.078	0.746	0.962	1.000	0.979	0.991	0.972	0.999	0.975
10	0.035	0.347	0.897	1.000	1.000	0.840	1.000	0.985	0.959	0.911
100	0.435	0.497	0.466	0.912	0.839	0.981	0.853	0.556	0.981	0.998
1000	0.988	0.997	0.007	0.414	0.379	0.057	0.440	0.611	0.168	0.461

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: (S)-(+)-Ketamine

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 106	100 $\pm$ 148	100 $\pm$ 119	100 $\pm$ 106	100 $\pm$ 123	100 $\pm$ 112	100 $\pm$ 144	100 $\pm$ 125	100 $\pm$ 115	100 $\pm$ 149	16
1	65 $\pm$ 103	61 $\pm$ 80	52 $\pm$ 53	100 $\pm$ 186	55 $\pm$ 67	66 $\pm$ 66	57 $\pm$ 69	43 $\pm$ 37	57 $\pm$ 49	37 $\pm$ 45	16
10	25 $\pm$ 44	21 $\pm$ 30	37 $\pm$ 62	44 $\pm$ 66	23 $\pm$ 46	40 $\pm$ 53	31 $\pm$ 49	45 $\pm$ 71	32 $\pm$ 31	23 $\pm$ 26	16
100	69 $\pm$ 106	42 $\pm$ 106	16 $\pm$ 57	11 $\pm$ 35	36 $\pm$ 113	19 $\pm$ 77	1 $\pm$ 3	0 $\pm$ 1	0 $\pm$ 0	1 $\pm$ 5	16
1000	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 1	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	16

Mean  $\pm$  standard deviation

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	47-153	26-174	41-159	47-153	38-162	44-156	28-172	37-163	42-158	26-174
1	14-117	21-101	25-78	7-193	22-88	33-99	23-92	24-61	32-82	15-60
10	3-47	6-35	6-68	12-77	0-46	13-66	6-55	9-80	16-47	10-36
100	16-121	-11-96	-13-45	-7-28	-21-92	-19-58	-12	0-1	0-0	-13
1000	0-0	0-0	0-0	0-1	0-0	0-0	0-0	0-0	0-0	0-0

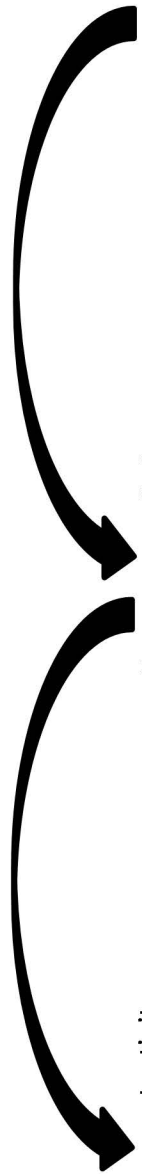
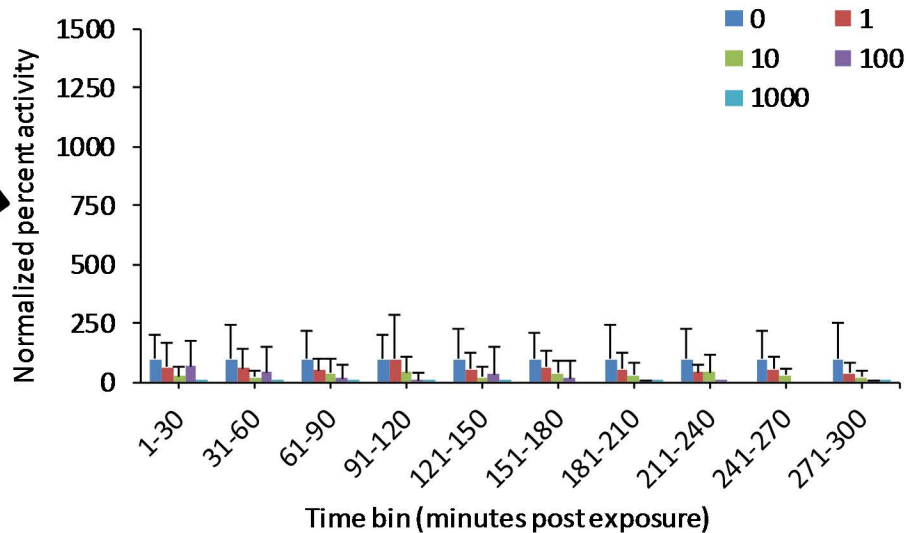
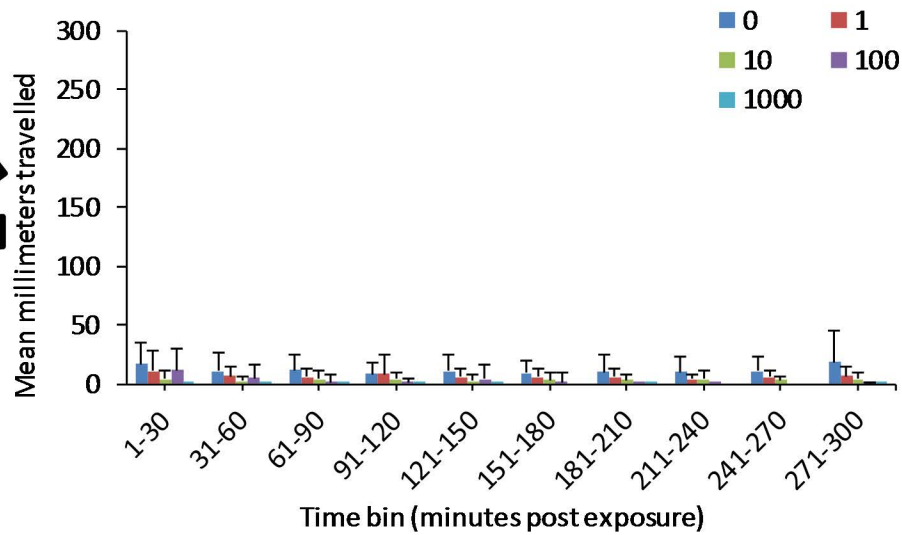
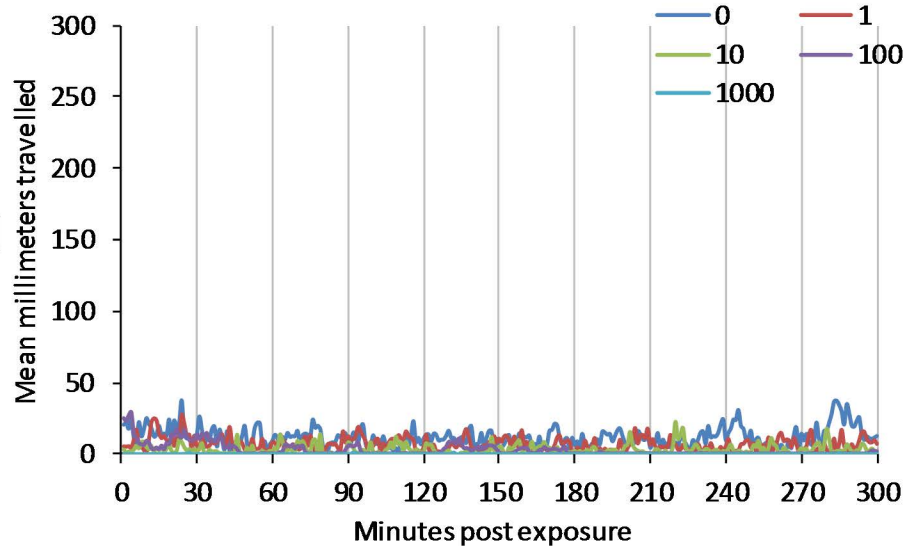
95% confidence interval

## p-values

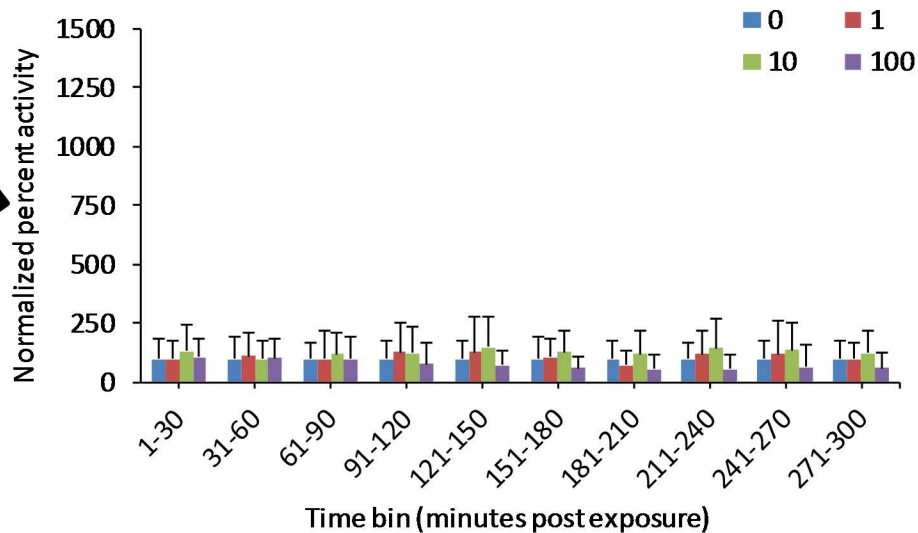
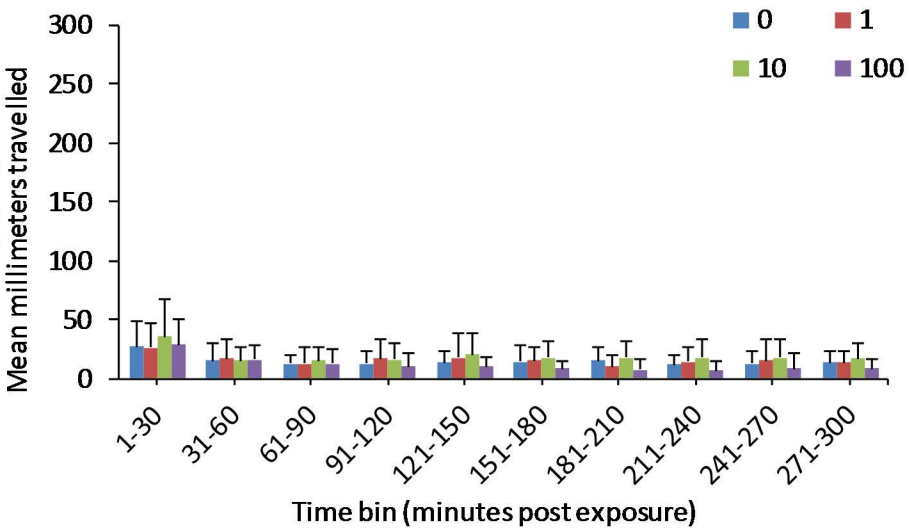
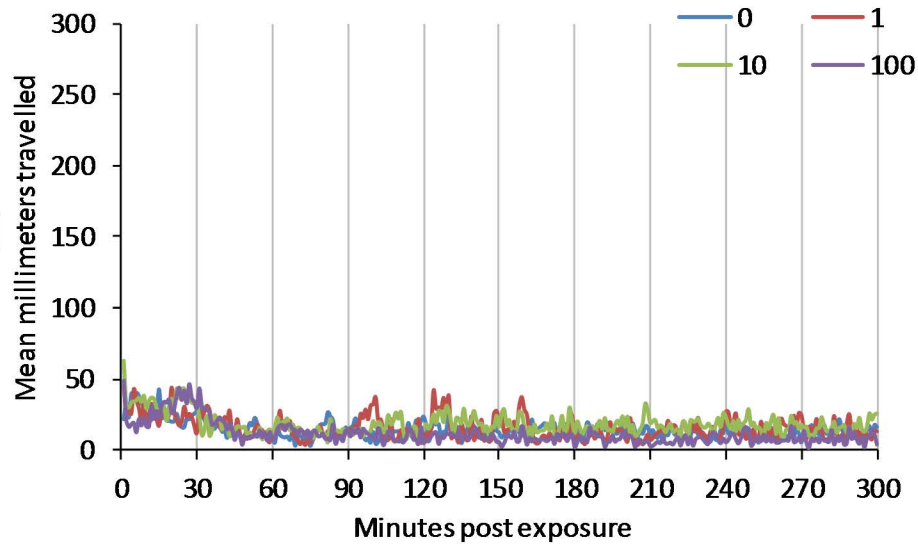
## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.009	0.968	0.989	0.738	0.952	1.000	0.893	0.697	0.905	0.900
10	0.001	0.043	0.024	0.057	0.004	0.180	0.065	0.066	0.236	0.409
100	0.039	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
1000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Mecamylamine



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 81	100 ± 90	100 ± 66	100 ± 75	100 ± 74	100 ± 96	100 ± 76	100 ± 66	100 ± 74	100 ± 73	24
1	98 ± 75	110 ± 102	99 ± 116	129 ± 124	130 ± 145	106 ± 77	71 ± 65	119 ± 98	120 ± 141	96 ± 75	22
10	130 ± 117	97 ± 76	120 ± 91	123 ± 115	150 ± 126	126 ± 94	119 ± 97	146 ± 123	137 ± 115	124 ± 95	23
100	107 ± 79	105 ± 80	99 ± 99	79 ± 90	72 ± 62	60 ± 51	54 ± 59	57 ± 64	66 ± 97	59 ± 67	21

## Mean ± standard deviation

† Exclusion: precipitation observed in 1000 μM treatment group

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	67-133	63-137	73-127	69-131	70-130	61-139	69-131	73-127	70-130	70-130
1	66-130	66-153	50-149	76-182	68-192	73-139	44-99	77-161	60-180	64-128
10	81-179	65-129	82-158	75-171	97-202	87-166	79-160	95-198	89-185	84-163
100	73-142	70-140	56-142	40-118	45-99	38-82	28-80	29-85	24-108	30-88

## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	1.000	1.000	0.678	0.998	0.867	0.972	0.389	1.000	0.985	0.999
10	0.656	0.992	0.947	0.925	0.357	0.588	0.983	0.767	0.747	0.724
100	0.898	0.984	0.926	0.500	0.600	0.450	0.034	0.035	0.049	0.116

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

**CHEMICAL: (+)-Methamphetamine**

**Normalized percent activity**

**Time bin (minutes post exposure)**

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 106	100 $\pm$ 90	100 $\pm$ 106	100 $\pm$ 85	100 $\pm$ 84	100 $\pm$ 96	100 $\pm$ 88	100 $\pm$ 77	100 $\pm$ 75	100 $\pm$ 74	16
1	127 $\pm$ 140	109 $\pm$ 143	12 $\pm$ 136	165 $\pm$ 259	119 $\pm$ 180	68 $\pm$ 73	128 $\pm$ 131	70 $\pm$ 74	37 $\pm$ 40	31 $\pm$ 45	16
10	35 $\pm$ 53	21 $\pm$ 49	14 $\pm$ 33	18 $\pm$ 47	4 $\pm$ 7	4 $\pm$ 4	5 $\pm$ 4	5 $\pm$ 6	2 $\pm$ 3	3 $\pm$ 3	16
100	1 $\pm$ 1	1 $\pm$ 2	1 $\pm$ 2	1 $\pm$ 2	1 $\pm$ 2	1 $\pm$ 2	6 $\pm$ 19	13 $\pm$ 44	4 $\pm$ 12	0 $\pm$ 1	16
1000	1 $\pm$ 2	0 $\pm$ 1	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	16

Mean  $\pm$  standard deviation

**Normalized percent activity**

**Time bin (minutes post exposure)**

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	47-153	55-145	47-153	57-143	58-142	52-148	56-144	62-138	63-137	63-137
1	57-197	37-131	44-130	35-294	29-209	32-105	38-219	33-107	17-56	9-54
10	9-61	-3-46	-2-30	-6-42	1-7	2-6	3-7	2-8	1-4	2-5
100	0-2	0-2	0-2	0-2	0-2	0-2	-3-16	-9-35	-3-10	0-1
1000	0-3	0-1	0-0	0-0	0-0	0-0	0-0	0-0	0-0	0-0

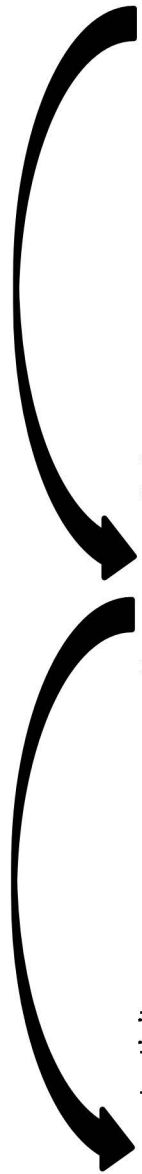
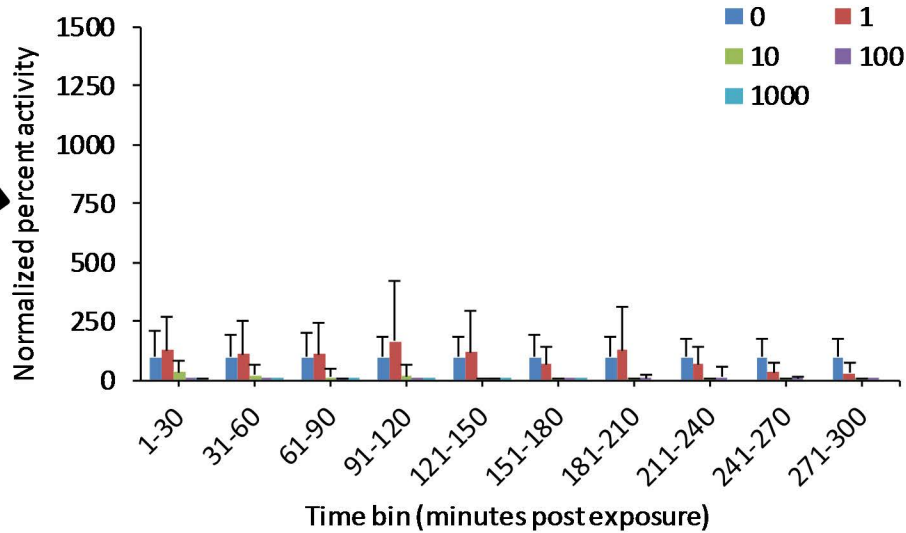
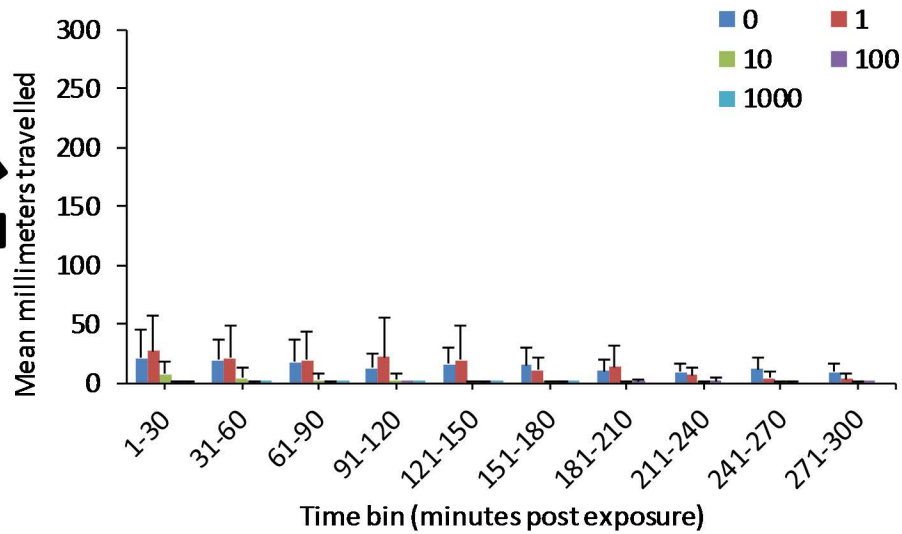
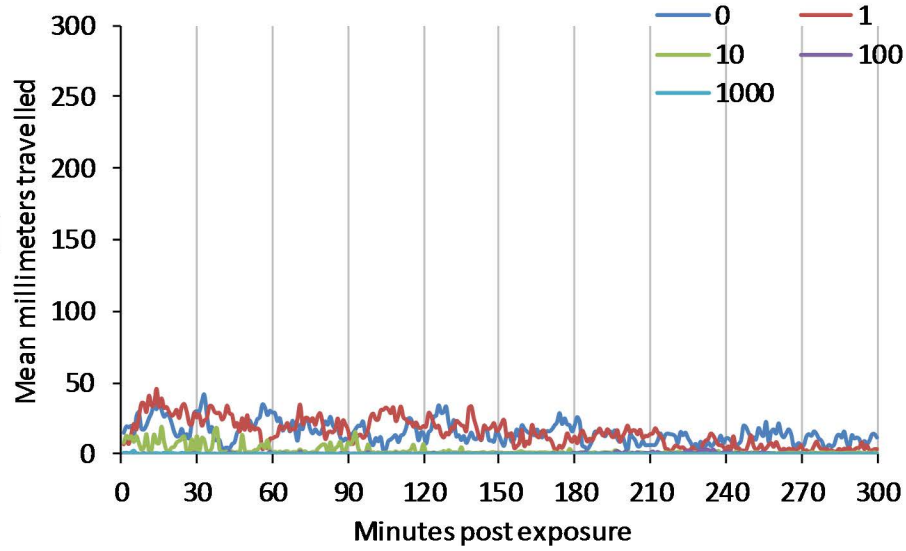
95% confidence interval

**p-values**

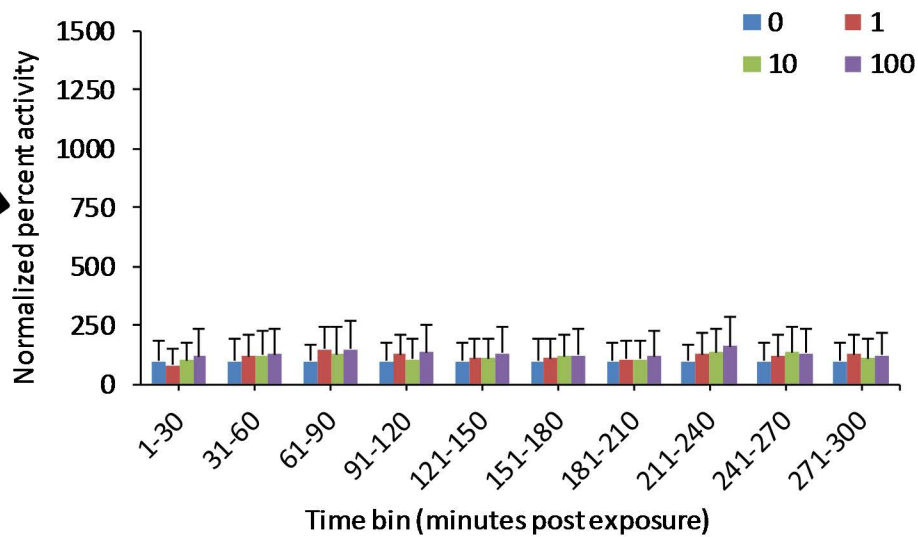
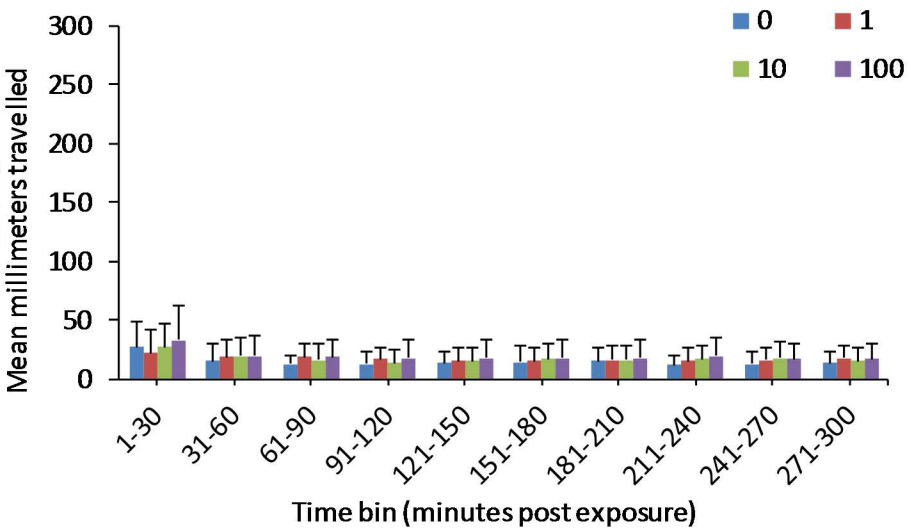
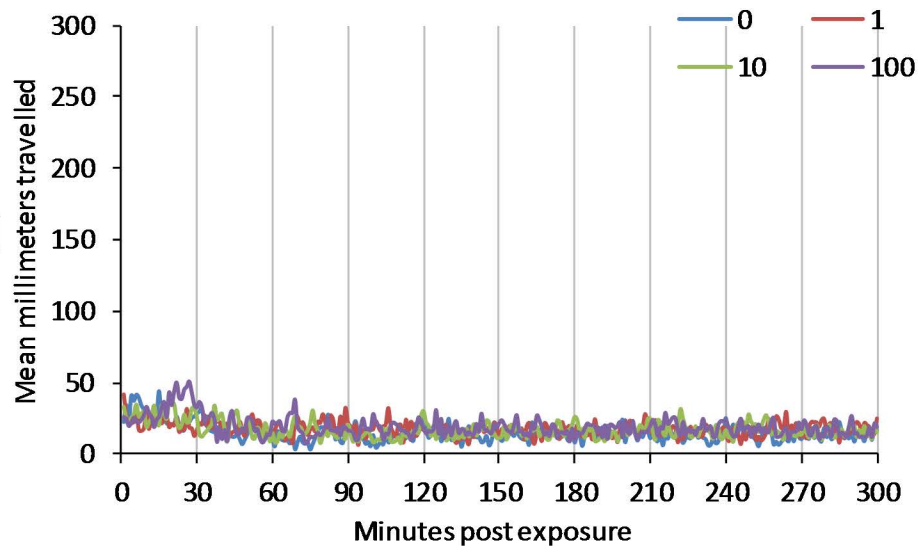
**Time bin (minutes post exposure)**

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.998	0.717	0.970	0.390	0.953	0.890	0.984	0.895	0.017	0.004
10	0.078	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
100	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
1000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Methyllycaconitine



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 81	100 ± 90	100 ± 66	100 ± 75	100 ± 74	100 ± 96	100 ± 76	100 ± 66	100 ± 74	100 ± 73	24
1	81 ± 71	120 ± 91	150 ± 92	130 ± 81	109 ± 87	110 ± 82	108 ± 81	127 ± 93	121 ± 91	130 ± 81	24
10	102 ± 72	124 ± 105	129 ± 112	105 ± 86	113 ± 83	118 ± 93	106 ± 81	138 ± 96	135 ± 109	112 ± 83	24
100	121 ± 111	128 ± 105	149 ± 122	138 ± 117	131 ± 117	124 ± 110	118 ± 109	161 ± 124	134 ± 100	122 ± 100	23

## Mean ± standard deviation

† Exclusion: precipitation observed in 1000 μM treatment group

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	67-133	63-137	73-127	69-131	70-130	61-139	69-131	73-127	70-130	70-130
1	52-110	83-158	112-188	97-163	74-145	76-143	75-141	90-165	84-158	97-163
10	72-131	81-167	83-175	70-140	79-147	80-155	73-139	99-178	91-160	78-146
100	74-167	84-171	98-200	90-187	83-180	78-170	73-164	109-213	92-175	81-164

## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.758	0.650	0.317	0.590	0.951	0.872	0.977	0.918	0.905	0.517
10	0.994	0.863	0.989	0.998	0.992	0.925	1.000	0.804	0.754	0.957
100	0.906	0.898	0.632	0.868	0.917	0.911	0.998	0.462	0.796	0.918

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: (-)-Nicotine

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 70	100 $\pm$ 86	100 $\pm$ 94	100 $\pm$ 85	100 $\pm$ 84	100 $\pm$ 94	100 $\pm$ 84	100 $\pm$ 83	100 $\pm$ 87	100 $\pm$ 84	27
1	295 $\pm$ 137	305 $\pm$ 194	185 $\pm$ 106	242 $\pm$ 117	204 $\pm$ 97	200 $\pm$ 93	205 $\pm$ 104	205 $\pm$ 81	157 $\pm$ 58	201 $\pm$ 59	28
10	81 $\pm$ 49	4 $\pm$ 11	14 $\pm$ 29	42 $\pm$ 64	36 $\pm$ 51	35 $\pm$ 46	41 $\pm$ 56	41 $\pm$ 56	34 $\pm$ 51	56 $\pm$ 81	30
100	3 $\pm$ 8	2 $\pm$ 7	0 $\pm$ 2	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	0 $\pm$ 0	1 $\pm$ 4	0 $\pm$ 0	29

## Mean $\pm$ standard deviation

<sup>‡</sup>Exclusion: lethality observed in 1000  $\mu$ M treatment group (30 of 30 animals)

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	73-127	67-133	64-136	67-133	68-132	64-136	68-132	68-132	67-133	68-132
1	243-347	232-379	145-225	198-286	167-241	165-235	166-244	174-236	135-179	179-223
10	63-99	0-8	4-25	19-65	17-55	19-52	21-62	20-61	16-53	26-85
100	-3-10	-14	0-1	0-0	0-0	0-0	0-0	0-0	-1-2	0-0

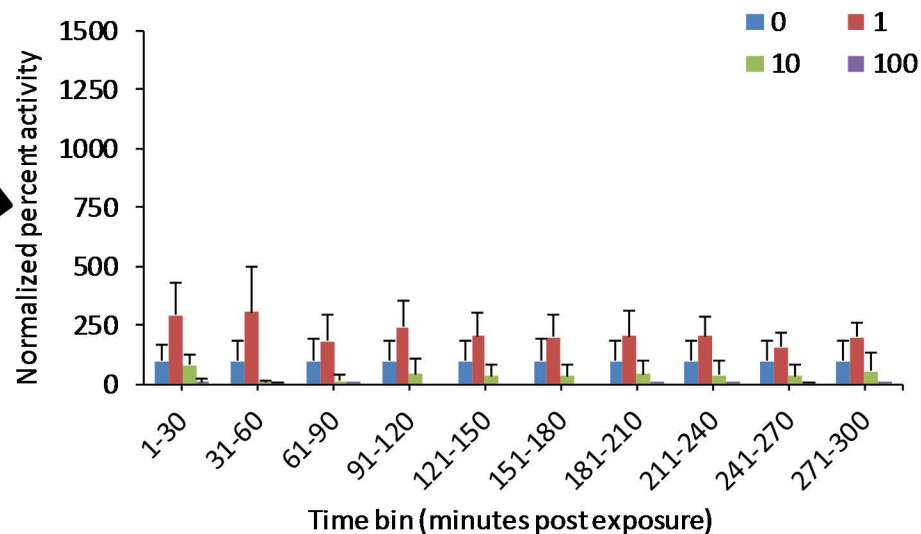
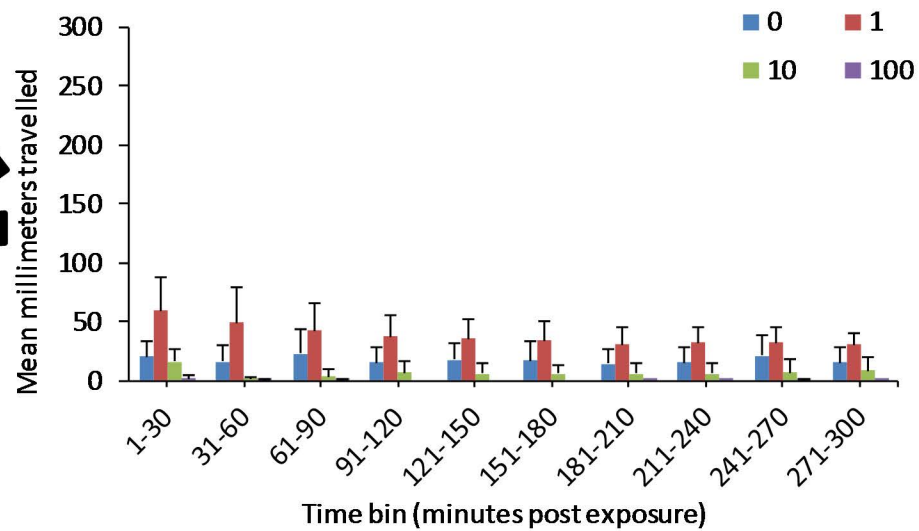
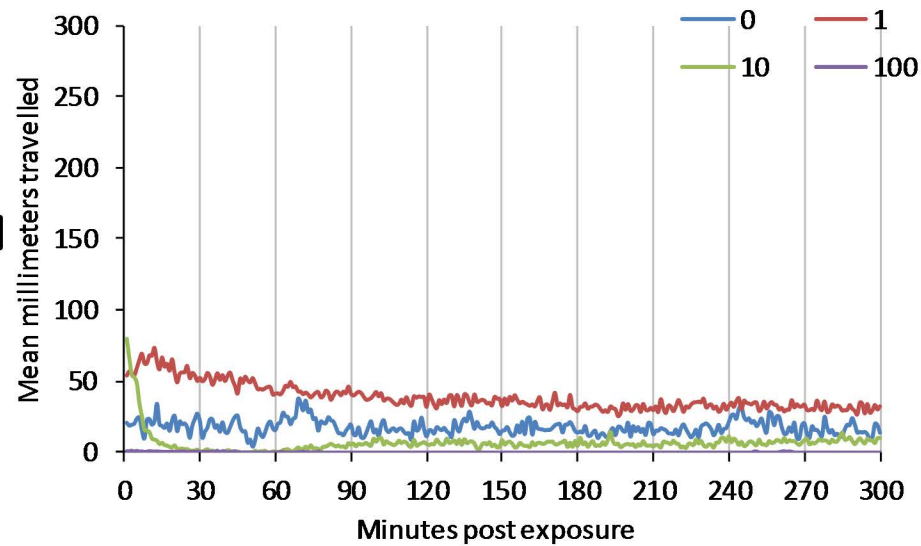
## 95% confidence interval

## p-values

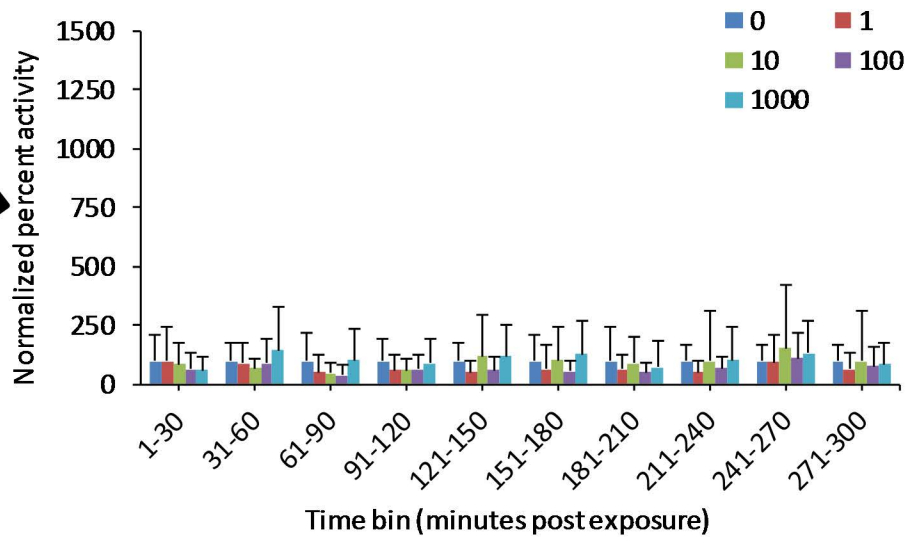
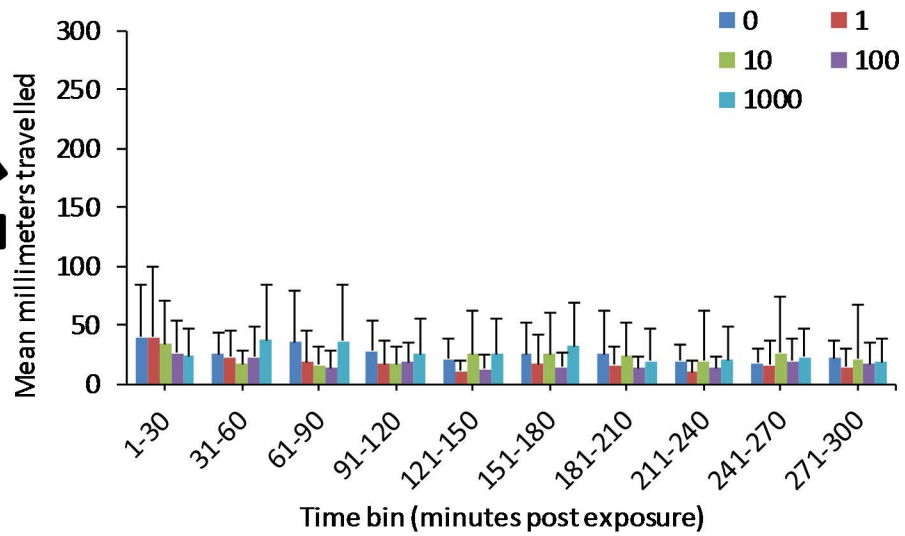
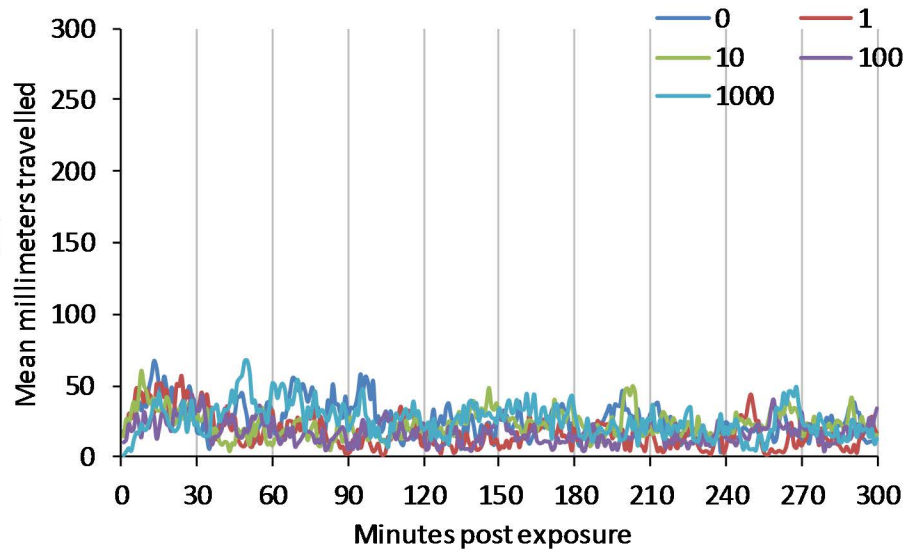
## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.008	0.001
10	0.971	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
100	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: N-methyl-D-aspartate (NMDA)



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 112	100 ± 73	100 ± 120	100 ± 90	100 ± 76	100 ± 108	100 ± 144	100 ± 69	100 ± 72	100 ± 68	16
1	99 ± 150	89 ± 88	53 ± 73	59 ± 69	51 ± 45	66 ± 100	63 ± 61	52 ± 49	93 ± 120	66 ± 69	16
10	84 ± 94	67 ± 45	46 ± 43	61 ± 51	120 ± 171	101 ± 141	91 ± 113	98 ± 213	152 ± 268	99 ± 210	16
100	65 ± 70	92 ± 103	38 ± 43	67 ± 56	61 ± 58	56 ± 48	53 ± 37	69 ± 45	111 ± 106	78 ± 79	16
1000	59 ± 58	147 ± 135	101 ± 131	91 ± 103	120 ± 136	128 ± 143	74 ± 109	101 ± 140	132 ± 139	84 ± 95	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	44-156	63-137	40-160	55-145	62-138	46-154	28-172	66-134	64-136	66-134
1	24-174	45-133	16-89	25-94	29-74	15-116	32-93	27-76	33-153	31-100
10	37-131	44-89	24-67	36-87	34-206	31-172	35-148	11-207	18-286	-6-203
100	30-100	40-143	17-60	39-95	32-90	32-80	35-72	46-91	58-164	39-118
1000	30-88	54-239	35-167	40-142	52-188	57-200	20-129	31-171	62-201	36-132

## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	1.000	0.999	0.430	0.780	0.834	0.908	0.870	0.873	1.000	0.945
10	0.968	0.917	0.294	0.813	0.993	1.000	0.999	1.000	0.894	1.000
100	0.624	1.000	0.170	0.880	0.919	0.798	0.746	0.972	1.000	0.990
1000	0.483	0.763	1.000	0.999	0.993	0.952	0.963	1.000	0.981	0.997

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



**CHEMICAL: Tricaine mesylate (MS-222)**

**Normalized percent activity**

	Time bin (minutes post exposure)										
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 92	100 ± 106	100 ± 97	100 ± 93	100 ± 84	100 ± 100	100 ± 86	100 ± 87	100 ± 73	100 ± 74	29
1	101 ± 71	156 ± 143	131 ± 121	139 ± 104	109 ± 82	125 ± 100	103 ± 82	130 ± 100	134 ± 82	111 ± 78	31
10	42 ± 51	99 ± 97	109 ± 101	92 ± 84	82 ± 75	111 ± 88	82 ± 81	94 ± 78	87 ± 69	95 ± 77	29
100	21 ± 22	64 ± 55	49 ± 58	41 ± 51	26 ± 27	18 ± 20	20 ± 30	24 ± 34	24 ± 35	25 ± 31	27

Mean ± standard deviation

‡ Exclusion: lethality observed in 1000  $\mu$ M treatment group (30 of 30 animals)

**Normalized percent activity**

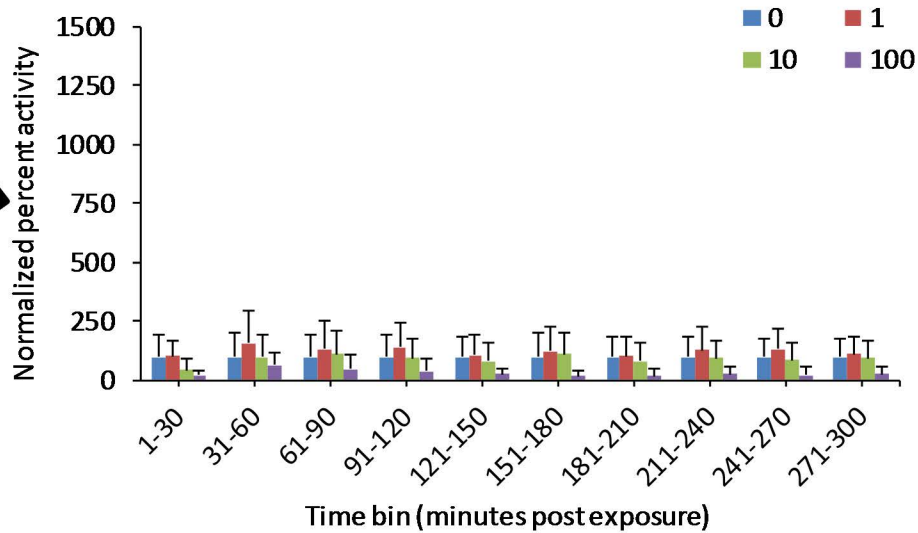
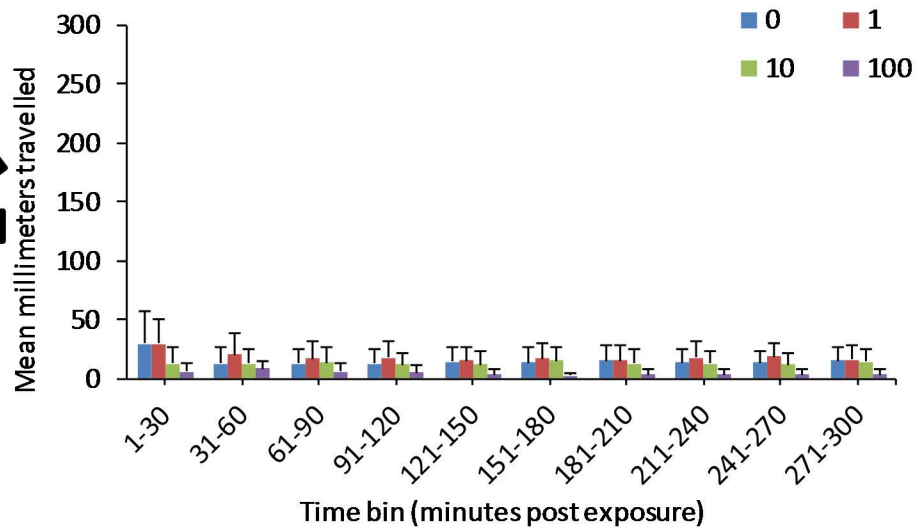
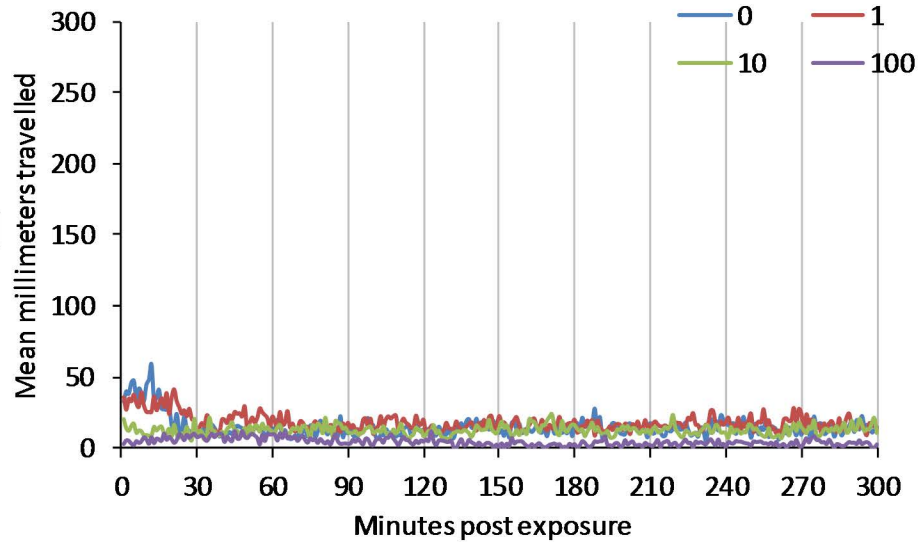
	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	66-134	61-139	64-136	65-135	69-131	63-137	68-132	68-132	73-127	72-128
1	76-126	105-207	87-174	102-177	79-138	90-161	73-132	94-166	104-163	82-139
10	23-60	63-135	72-147	61-123	54-110	79-144	52-112	65-123	61-112	66-123
100	13-30	43-86	27-71	21-60	15-36	10-26	8-31	11-38	10-37	13-37

95% confidence interval

**p-values**

	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.847	0.108	0.493	0.286	0.902	0.502	0.920	0.565	0.455	0.904
10	0.001	1.000	0.996	0.977	0.844	0.911	0.705	0.996	0.878	0.990
100	0.001	0.656	0.080	0.006	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# GABA agonists and positive modulators

## **10 tested chemicals:**

Alfaxalone (5 $\alpha$ -pregnan-3 $\alpha$ -ol-11,20-dione)

( $\pm$ )-Baclofen

Carbamazepine

CGP 13501

Chlormethiazole

Ethanol

gamma-Aminobutyric Acid (GABA)

Muscimol

SKF 97541 (CGP 35024)

Valproic Acid

**CHEMICAL: Alfaxalone (5 $\alpha$ -pregnan-3 $\alpha$ -ol-11,20-dione )**

**Normalized percent activity**      **Time bin (minutes post exposure)**

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 52	100 $\pm$ 59	100 $\pm$ 108	100 $\pm$ 78	100 $\pm$ 60	100 $\pm$ 70	100 $\pm$ 69	100 $\pm$ 70	100 $\pm$ 57	100 $\pm$ 60	19
1	66 $\pm$ 31	77 $\pm$ 36	63 $\pm$ 30	96 $\pm$ 46	92 $\pm$ 42	99 $\pm$ 66	92 $\pm$ 51	94 $\pm$ 56	112 $\pm$ 64	98 $\pm$ 58	24
10	1 $\pm$ 1	2 $\pm$ 8	2 $\pm$ 8	0 $\pm$ 0	0 $\pm$ 1	0 $\pm$ 1	1 $\pm$ 2	1 $\pm$ 2	2 $\pm$ 5	1 $\pm$ 2	21

Mean  $\pm$  standard deviation

<sup>†</sup> Exclusion: precipitation observed in 100 and 1000  $\mu$ M treatment groups

**Normalized percent activity**      **Time bin (minutes post exposure)**

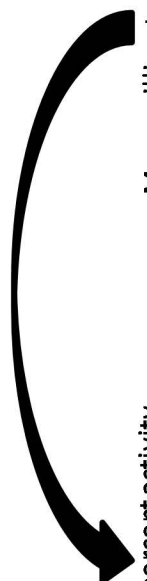
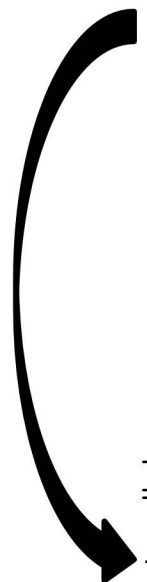
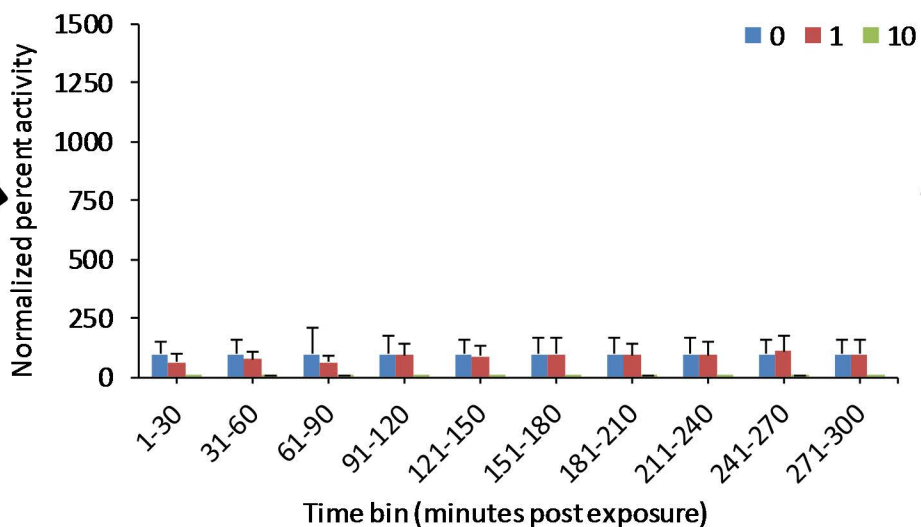
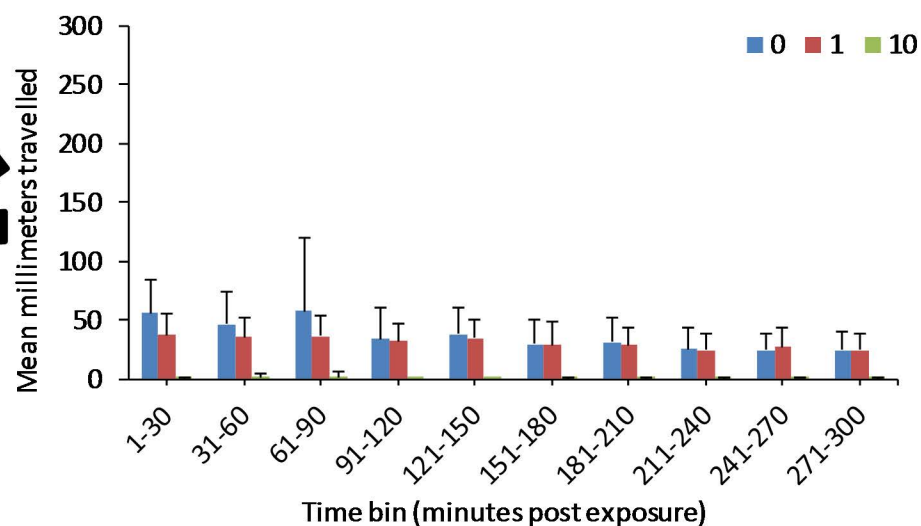
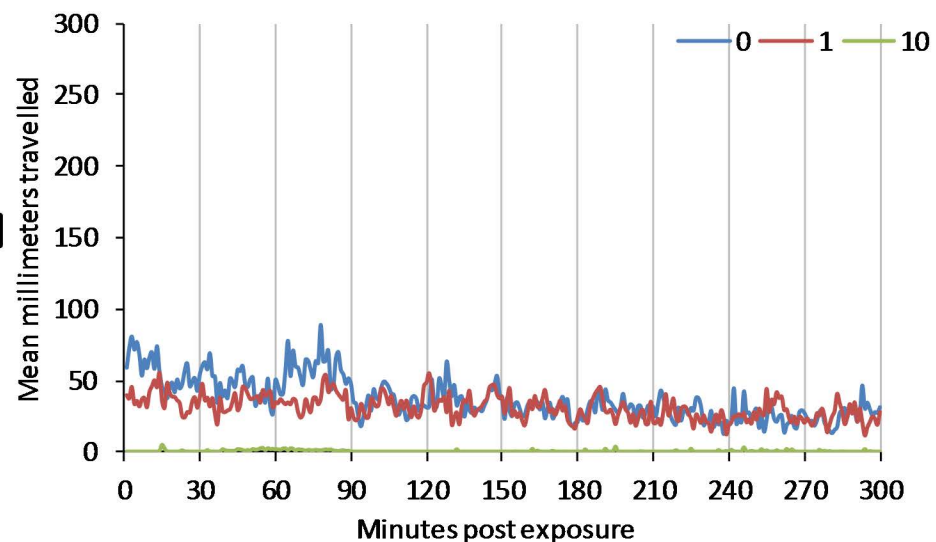
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	76-124	73-127	51-149	64-136	73-127	68-132	68-132	68-132	74-126	72-128
1	54-79	62-91	51-75	77-114	75-109	73-126	71-113	72-117	86-138	74-122
10	0-1	-16	-16	0-0	0-0	0-1	0-2	0-1	0-4	0-1

95% confidence interval

**p-values**      **Time bin (minutes post exposure)**

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.054	0.437	0.400	0.858	1.000	1.000	0.999	0.985	0.858	0.986
10	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



**CHEMICAL: (±)-Baclofen**

**Normalized percent activity**

**Time bin (minutes post exposure)**

[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 85	100 ± 92	100 ± 87	100 ± 93	100 ± 79	100 ± 84	100 ± 80	100 ± 75	100 ± 90	100 ± 66	16
1	52 ± 43	51 ± 29	56 ± 33	56 ± 51	44 ± 40	65 ± 53	44 ± 35	55 ± 34	44 ± 35	52 ± 31	16
10	46 ± 23	50 ± 28	55 ± 27	58 ± 34	41 ± 25	57 ± 32	58 ± 48	63 ± 55	57 ± 24	51 ± 31	14
100	74 ± 61	82 ± 58	98 ± 71	103 ± 86	74 ± 72	67 ± 57	68 ± 60	75 ± 66	71 ± 64	70 ± 50	14
1000	102 ± 47	92 ± 81	41 ± 47	37 ± 31	40 ± 35	29 ± 25	29 ± 37	37 ± 32	36 ± 35	34 ± 33	16

**Mean ± standard deviation**

**Normalized percent activity**

**Time bin (minutes post exposure)**

[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	58-142	54-146	57-143	53-147	61-139	58-142	60-140	62-138	55-145	67-133
1	30-73	36-65	40-73	30-82	24-64	39-92	26-61	38-72	26-61	37-68
10	33-58	35-65	40-69	40-76	28-55	40-74	32-83	34-93	44-70	34-67
100	41-107	51-113	60-136	57-148	36-113	36-97	36-100	40-111	37-105	44-97
1000	79-126	52-133	18-65	21-52	23-58	17-42	11-47	21-53	18-53	18-51

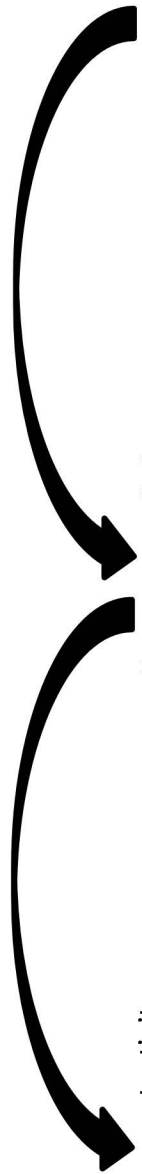
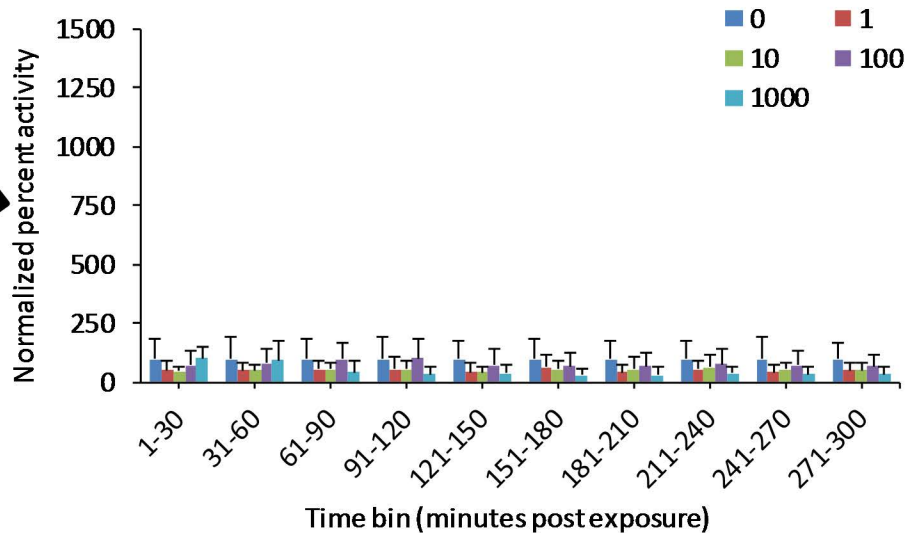
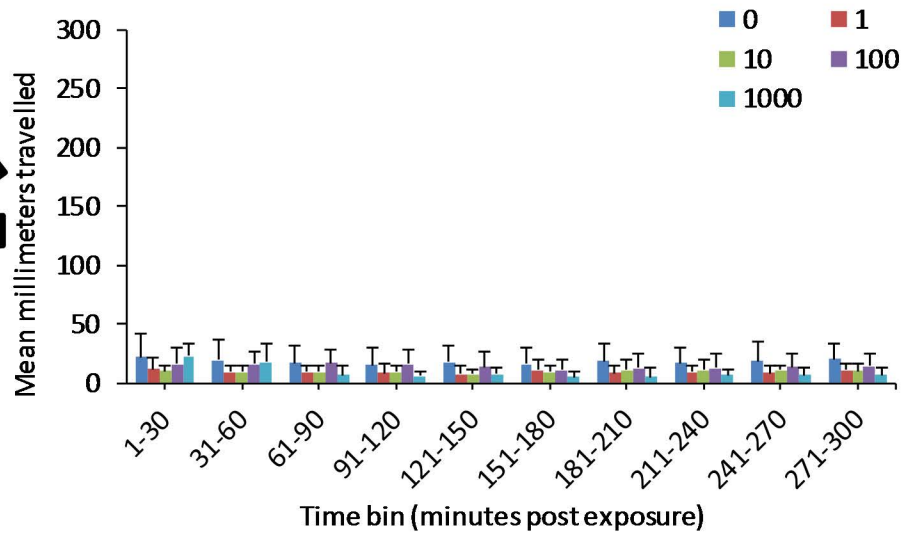
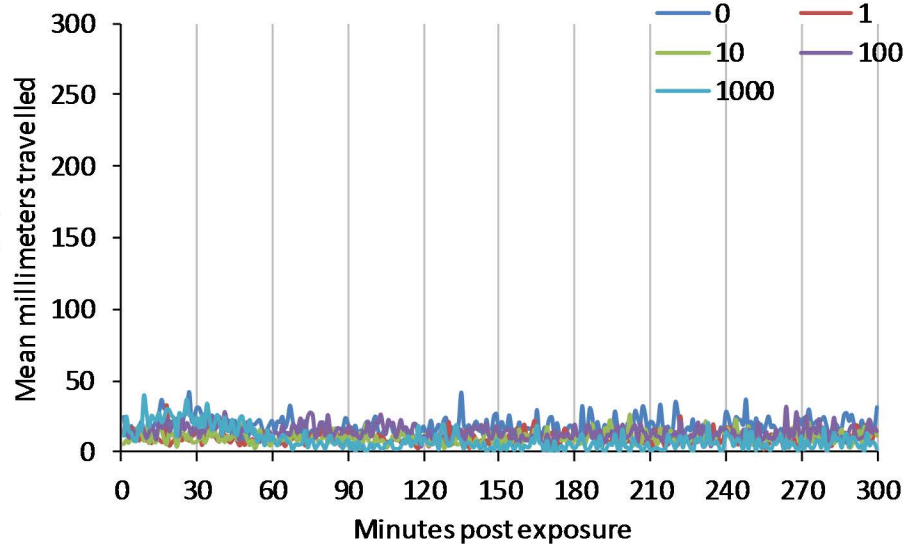
**95% confidence interval**

**p-values**

**Time bin (minutes post exposure)**

[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.155	0.426	0.530	0.593	0.097	0.623	0.094	0.408	0.315	0.204
10	0.198	0.469	0.689	0.688	0.130	0.628	0.439	0.626	0.976	0.173
100	0.908	1.000	0.999	1.000	0.806	0.643	0.682	0.803	0.982	0.651
1000	0.908	1.000	0.006	0.026	0.026	0.001	0.001	0.009	0.057	0.001

**Two-way repeated measures ANOVA, Tukey's post-hoc, p ≤ 0.05**



# CHEMICAL: Carbamazepine

## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 53	100 $\pm$ 70	100 $\pm$ 66	100 $\pm$ 67	100 $\pm$ 68	100 $\pm$ 71	100 $\pm$ 61	100 $\pm$ 60	100 $\pm$ 66	100 $\pm$ 66	24
1	61 $\pm$ 33	58 $\pm$ 44	79 $\pm$ 68	68 $\pm$ 53	64 $\pm$ 47	59 $\pm$ 48	72 $\pm$ 55	66 $\pm$ 45	87 $\pm$ 62	75 $\pm$ 59	23
10	78 $\pm$ 55	83 $\pm$ 55	85 $\pm$ 54	78 $\pm$ 62	62 $\pm$ 36	75 $\pm$ 43	69 $\pm$ 45	71 $\pm$ 44	89 $\pm$ 66	99 $\pm$ 50	22
100	54 $\pm$ 27	58 $\pm$ 38	51 $\pm$ 32	44 $\pm$ 28	38 $\pm$ 21	40 $\pm$ 26	42 $\pm$ 24	29 $\pm$ 22	48 $\pm$ 29	36 $\pm$ 30	24
1000	24 $\pm$ 14	15 $\pm$ 16	17 $\pm$ 28	14 $\pm$ 23	10 $\pm$ 24	6 $\pm$ 15	6 $\pm$ 18	1 $\pm$ 7	0 $\pm$ 0	0 $\pm$ 0	24

## Mean $\pm$ standard deviation

## Normalized percent activity

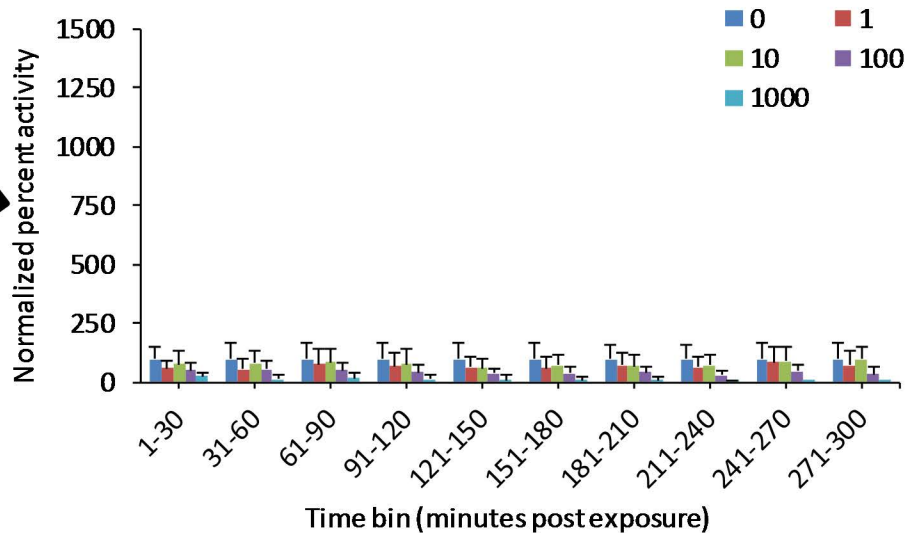
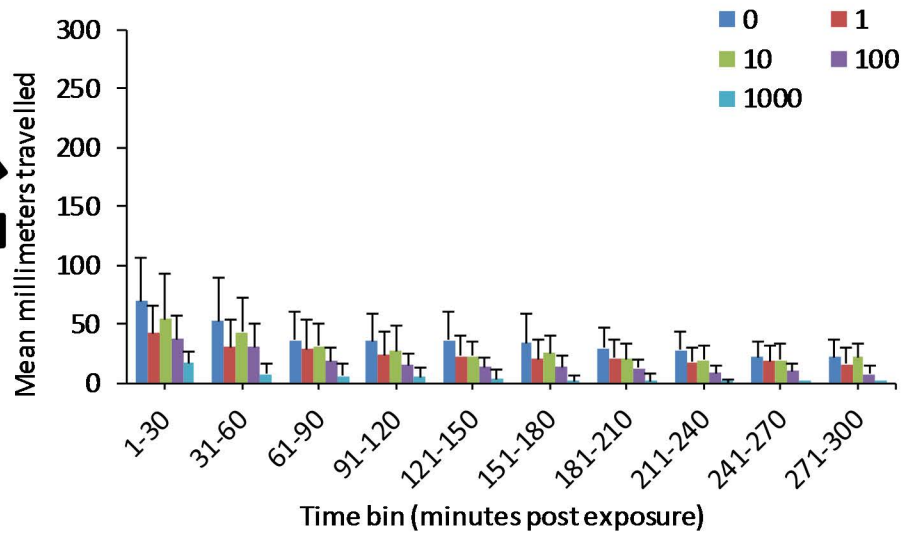
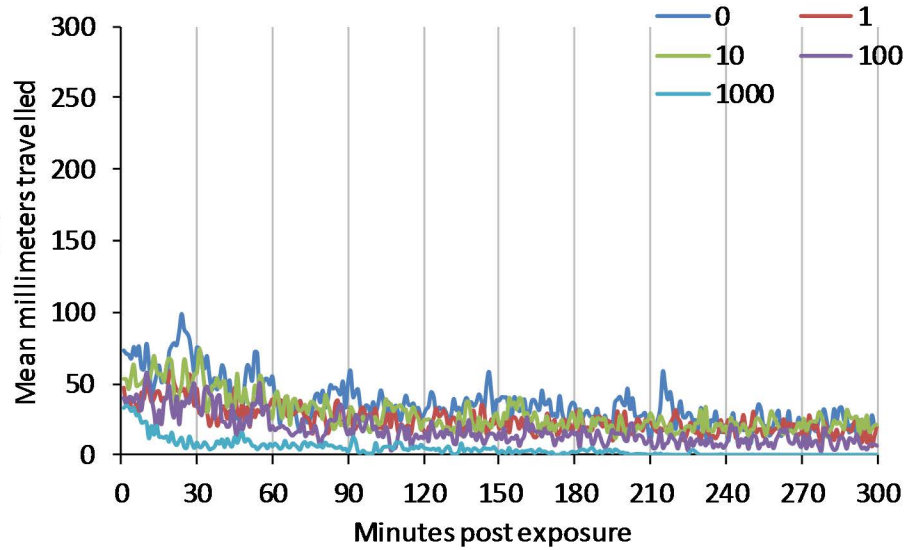
	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	78-122	71-129	73-127	73-127	72-128	71-129	75-125	75-125	73-127	73-127
1	47-75	39-76	50-107	46-91	44-83	39-79	49-95	47-84	61-113	50-100
10	54-101	60-107	62-108	51-104	46-77	57-93	50-88	52-90	61-117	78-120
100	42-65	42-73	38-64	32-56	30-47	29-50	32-52	20-38	36-60	24-49
1000	19-30	8-21	5-28	4-23	0-19	-1-12	-1-14	-14	0-0	0-0

## 95% confidence interval

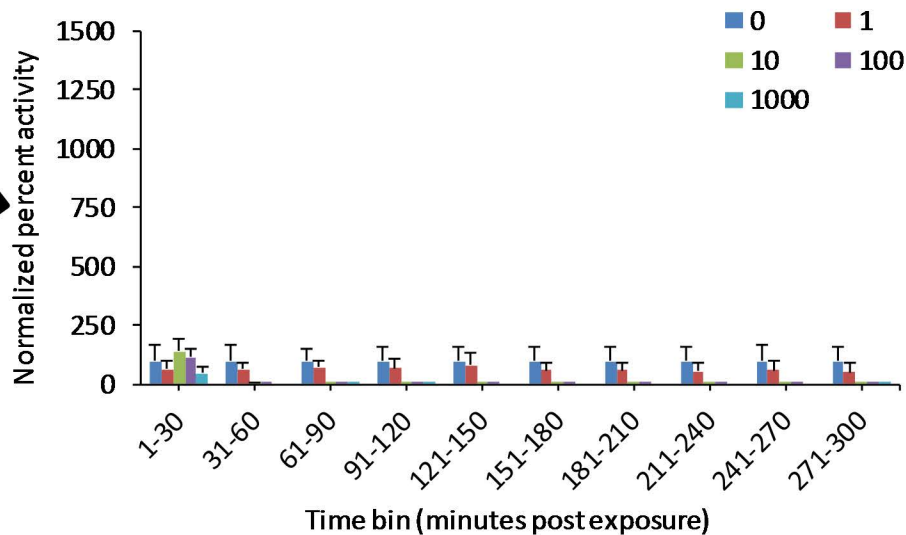
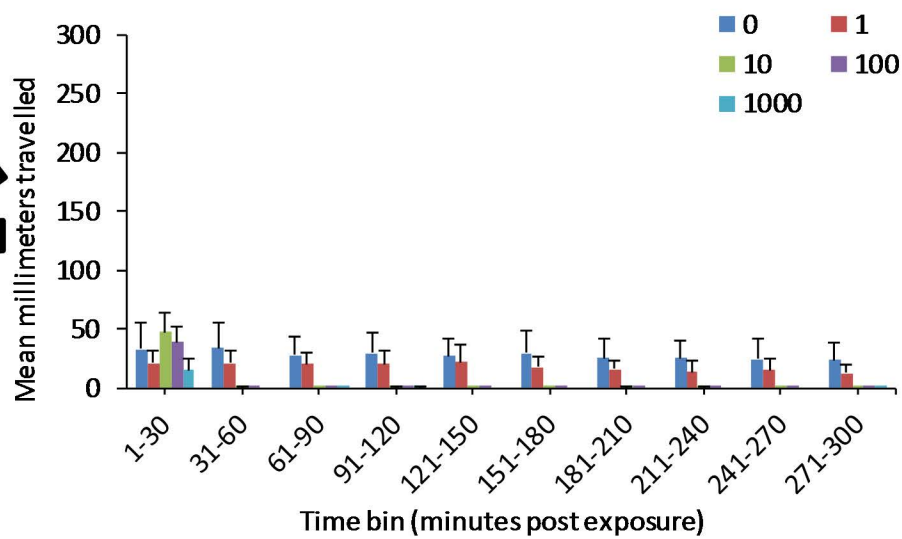
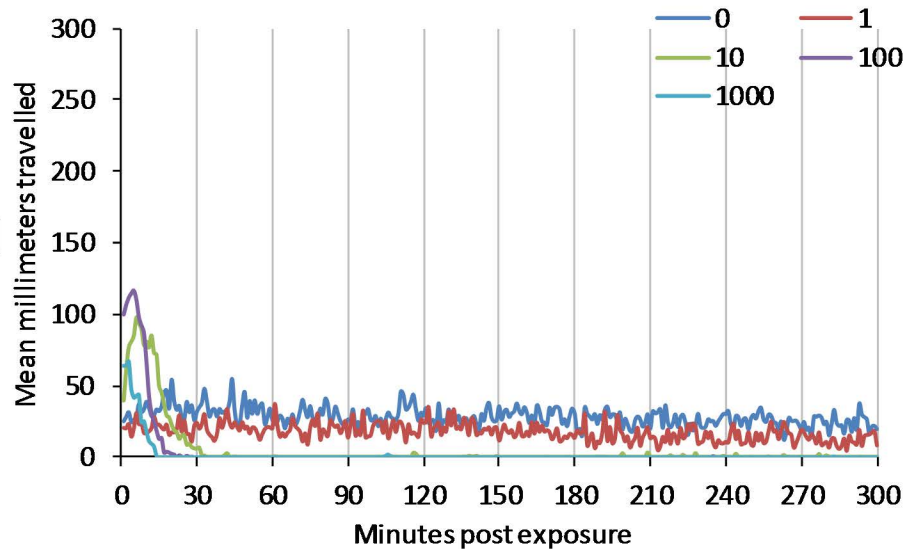
## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.025	0.053	0.707	0.365	0.217	0.163	0.512	0.333	0.992	0.697
10	0.309	0.959	0.991	0.481	0.230	0.891	0.427	0.558	0.975	0.998
100	0.002	0.080	0.025	0.002	0.001	0.001	0.002	0.001	0.022	0.001
1000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



**CHEMICAL: CGP 13501**



**Normalized percent activity**

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 65	100 ± 64	100 ± 51	100 ± 59	100 ± 58	100 ± 62	100 ± 60	100 ± 61	100 ± 68	100 ± 63	16
1	63 ± 34	62 ± 32	71 ± 32	70 ± 36	81 ± 57	59 ± 33	62 ± 29	55 ± 36	62 ± 39	53 ± 35	16
10	142 ± 50	1 ± 3	0 ± 0	1 ± 2	0 ± 1	0 ± 0	1 ± 2	1 ± 2	0 ± 1	0 ± 1	15
100	117 ± 38	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	16
1000	47 ± 27	0 ± 0	0 ± 0	0 ± 1	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	16

**Mean ± standard deviation**

**Normalized percent activity**

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	67-133	68-132	74-126	70-130	71-129	69-131	70-130	70-130	66-134	69-131
1	46-80	46-79	55-88	52-88	52-109	43-76	48-76	37-73	43-81	35-70
10	117-168	0-3	0-0	0-2	0-1	0-0	0-2	0-2	0-1	0-1
100	98-136	0-0	0-0	0-0	0-0	0-0	0-0	0-0	0-0	0-0
1000	33-60	0-0	0-0	0-1	0-0	0-0	0-0	0-0	0-0	0-0

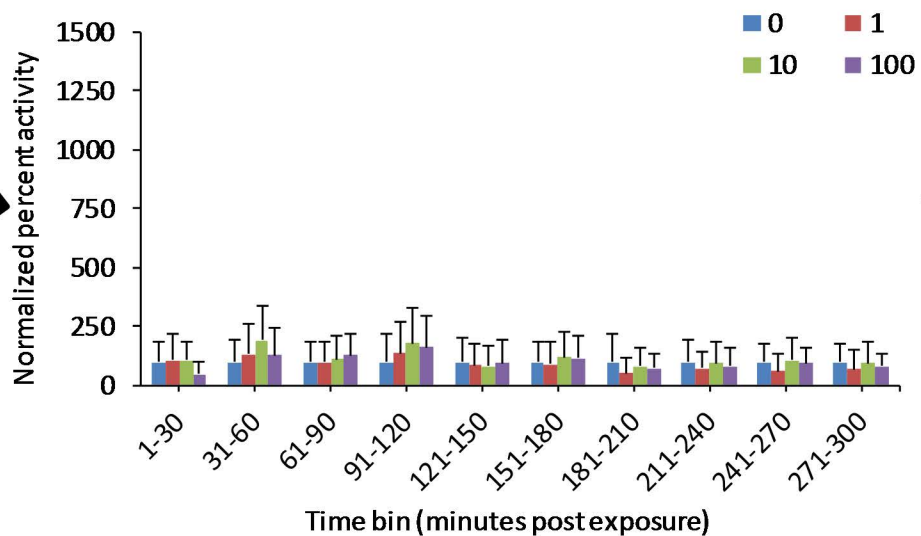
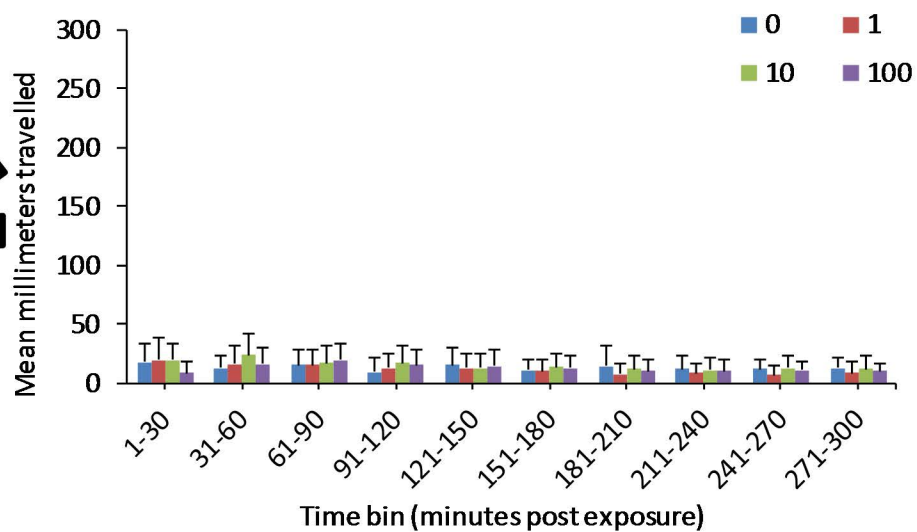
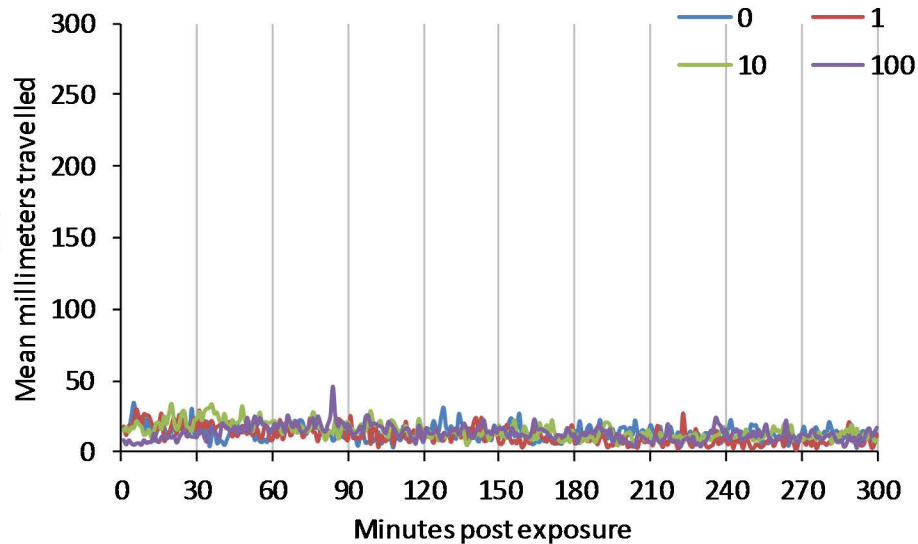
**95% confidence interval**

**p-values**

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.069	0.206	0.621	0.799	0.717	0.304	0.661	0.177	0.550	0.095
10	0.170	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
100	0.459	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
1000	0.023	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Chlormethiazole



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 82	100 ± 90	100 ± 84	100 ± 120	100 ± 101	100 ± 82	100 ± 121	100 ± 94	100 ± 76	100 ± 75	23
1	109 ± 109	132 ± 131	97 ± 91	137 ± 130	85 ± 88	89 ± 95	53 ± 68	72 ± 71	58 ± 74	68 ± 81	21
10	108 ± 78	190 ± 148	111 ± 98	178 ± 148	83 ± 82	118 ± 107	82 ± 76	92 ± 91	105 ± 93	93 ± 93	22
100	47 ± 54	128 ± 119	128 ± 90	160 ± 137	96 ± 95	114 ± 95	73 ± 62	83 ± 79	94 ± 66	81 ± 57	24

## Mean ± standard deviation

‡ Exclusion: lethality observed in 1000 μM treatment group (24 of 24 animals)

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	66-134	62-138	65-135	50-150	58-142	66-134	50-150	61-139	68-132	69-131
1	61-156	75-190	58-137	81-194	46-123	48-130	23-82	41-103	26-90	33-103
10	75-141	127-253	69-153	115-241	48-118	72-164	49-115	54-131	66-145	53-133
100	25-69	79-177	92-165	104-216	57-135	75-153	47-98	51-115	67-121	58-105

## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.947	0.918	0.929	0.650	0.847	0.915	0.290	0.802	0.147	0.335
10	0.973	0.071	0.999	0.058	0.934	0.891	1.000	0.983	1.000	0.966
100	0.016	0.899	0.734	0.254	0.999	0.992	0.956	0.922	0.994	0.953

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Ethanol

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 88	100 $\pm$ 94	100 $\pm$ 118	100 $\pm$ 139	100 $\pm$ 159	100 $\pm$ 155	100 $\pm$ 173	100 $\pm$ 155	100 $\pm$ 140	100 $\pm$ 80	16
1	74 $\pm$ 57	134 $\pm$ 124	111 $\pm$ 96	66 $\pm$ 63	92 $\pm$ 93	51 $\pm$ 29	97 $\pm$ 128	63 $\pm$ 52	100 $\pm$ 151	332 $\pm$ 531	16
10	67 $\pm$ 70	124 $\pm$ 181	63 $\pm$ 58	75 $\pm$ 99	93 $\pm$ 147	31 $\pm$ 23	52 $\pm$ 46	44 $\pm$ 48	85 $\pm$ 140	94 $\pm$ 85	16
100	78 $\pm$ 104	76 $\pm$ 89	70 $\pm$ 68	42 $\pm$ 36	91 $\pm$ 103	78 $\pm$ 110	89 $\pm$ 160	50 $\pm$ 52	58 $\pm$ 67	122 $\pm$ 137	16
1000	85 $\pm$ 92	61 $\pm$ 63	126 $\pm$ 137	70 $\pm$ 57	50 $\pm$ 43	51 $\pm$ 36	100 $\pm$ 164	70 $\pm$ 53	61 $\pm$ 59	182 $\pm$ 218	16

## Mean $\pm$ standard deviation

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	56-144	53-147	41-159	31-169	20-180	22-178	14-186	23-177	30-170	60-140
1	45-102	72-196	63-159	35-98	45-138	37-66	33-161	37-89	24-175	67-598
10	32-102	34-215	34-92	26-125	19-167	19-43	29-75	20-68	15-155	52-137
100	26-130	32-121	36-104	24-60	40-143	22-133	9-169	24-76	25-92	54-191
1000	39-131	30-93	58-195	41-98	29-72	33-69	18-182	44-97	32-91	73-291

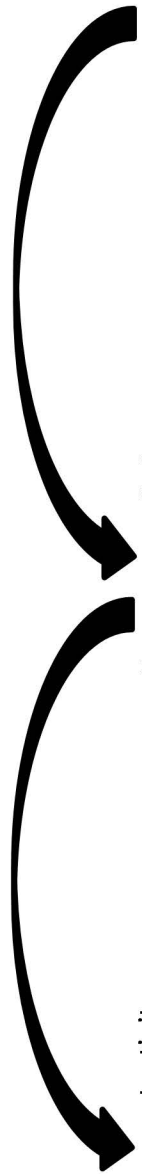
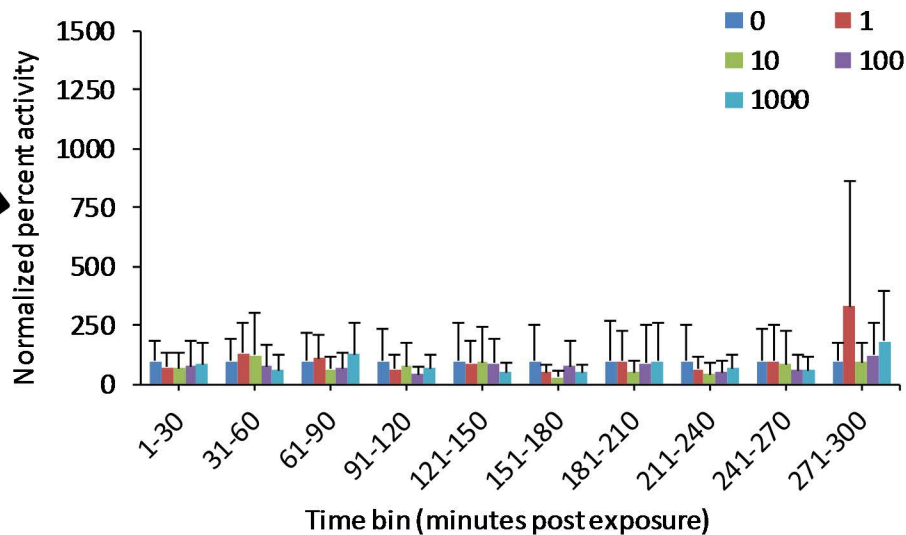
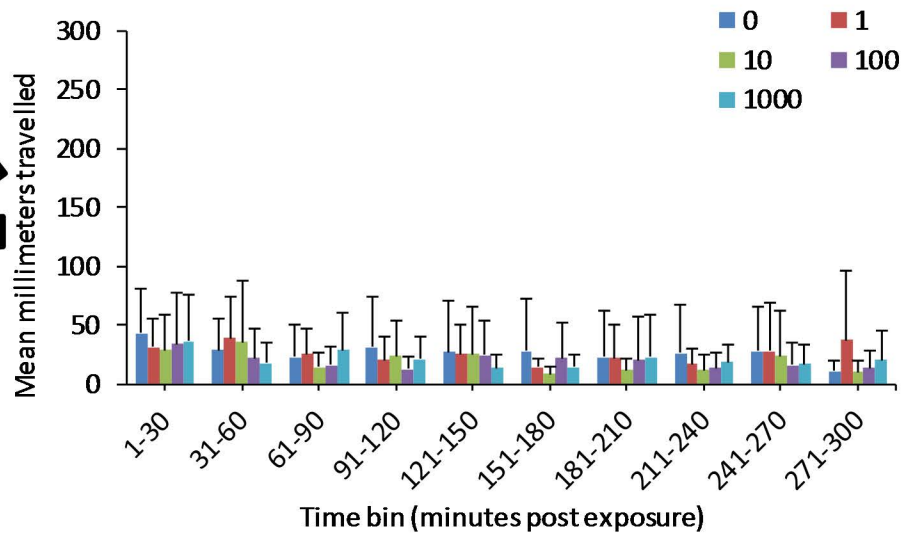
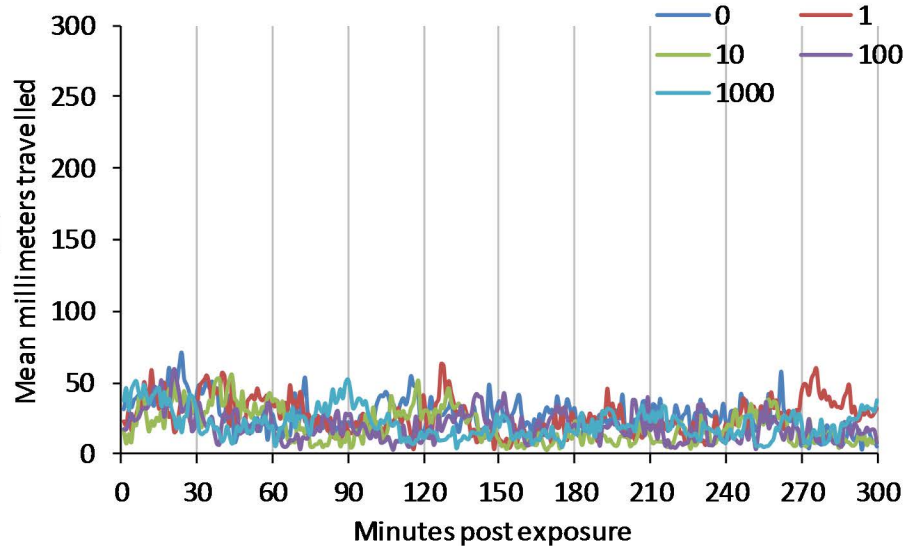
## 95% confidence interval

## p-values

## Time bin (minutes post exposure)

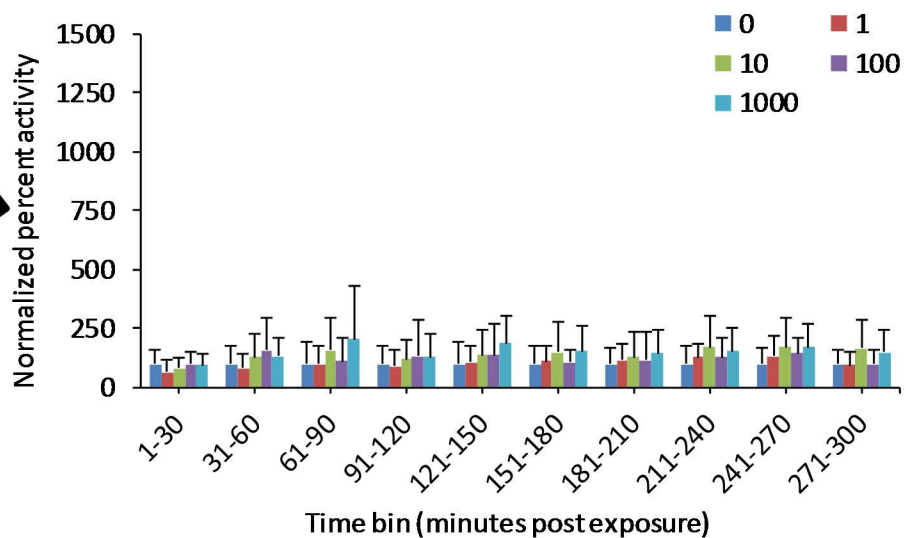
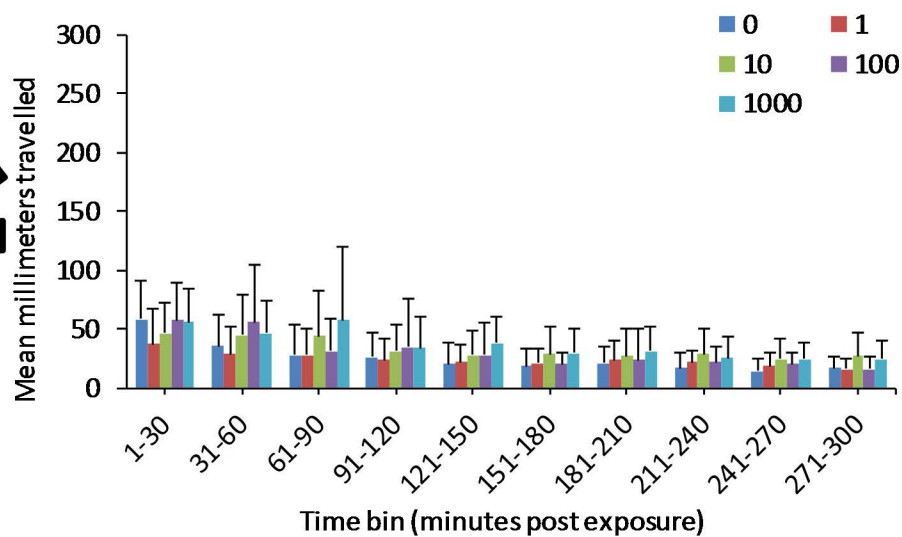
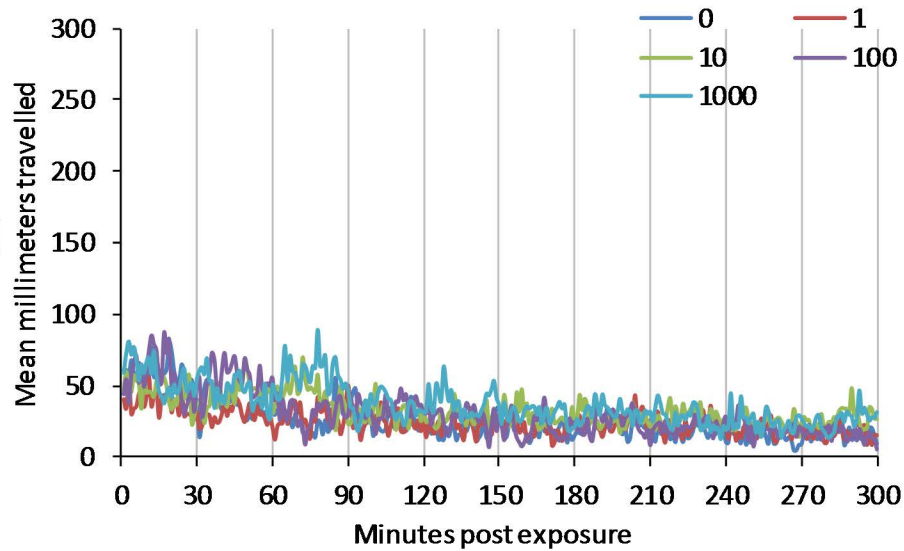
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.985	0.749	0.944	0.999	0.959	0.992	0.986	0.998	0.996	0.221
10	0.571	1.000	0.968	1.000	0.971	0.609	0.972	0.560	1.000	0.999
100	0.572	0.944	1.000	0.963	0.999	1.000	0.975	0.601	0.977	1.000
1000	0.976	0.570	0.988	0.993	0.813	0.976	1.000	1.000	0.993	0.837

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$





# CHEMICAL: gamma-Aminobutyric Acid (GABA)



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 56	100 ± 74	100 ± 92	100 ± 79	100 ± 91	100 ± 79	100 ± 65	100 ± 76	100 ± 71	100 ± 60	23
1	64 ± 51	82 ± 63	100 ± 78	90 ± 66	108 ± 70	110 ± 69	113 ± 76	129 ± 57	130 ± 84	95 ± 57	22
10	79 ± 44	127 ± 100	158 ± 138	119 ± 85	138 ± 105	151 ± 124	128 ± 107	170 ± 131	171 ± 121	165 ± 123	20
100	98 ± 56	157 ± 138	113 ± 99	132 ± 152	137 ± 135	108 ± 50	113 ± 121	129 ± 79	144 ± 67	98 ± 57	23
1000	96 ± 50	133 ± 79	206 ± 222	128 ± 100	139 ± 112	155 ± 109	146 ± 101	152 ± 106	171 ± 98	150 ± 91	19

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	77-123	69-131	62-138	67-133	62-138	67-133	73-127	68-132	70-130	75-125
1	42-86	55-109	66-133	62-118	78-138	81-140	81-145	105-153	94-167	70-119
10	60-99	82-171	96-220	81-157	92-185	95-207	81-176	112-228	116-225	110-220
100	75-121	100-215	72-154	69-196	81-193	87-129	63-164	97-162	116-172	74-122
1000	73-119	97-169	104-308	82-173	137-240	105-205	100-192	103-200	126-217	108-192

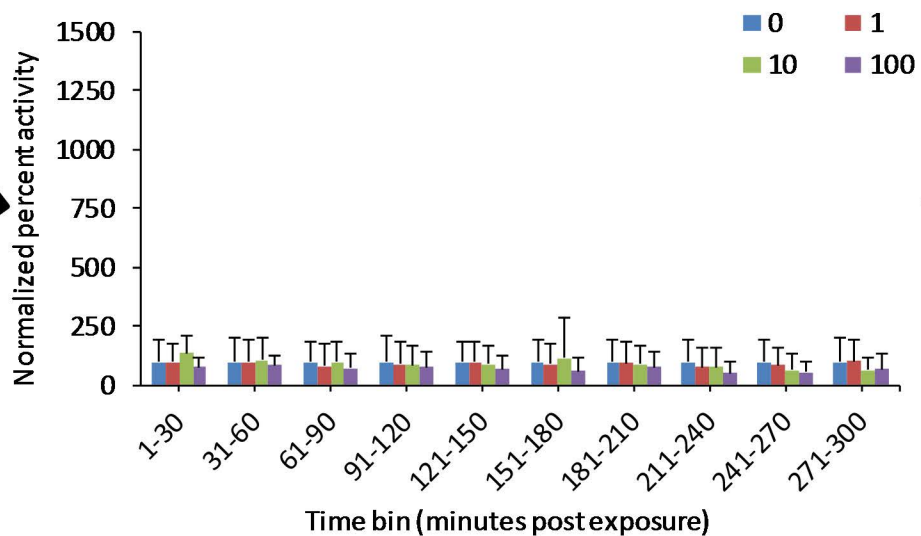
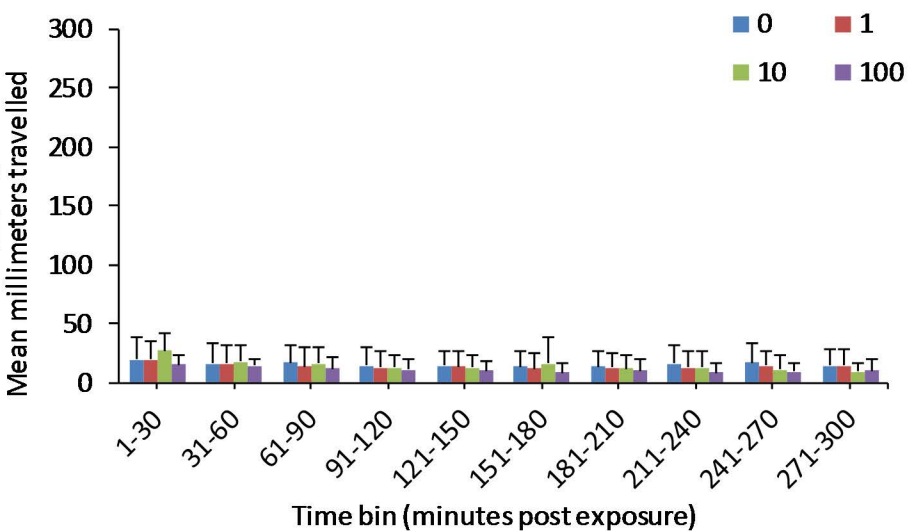
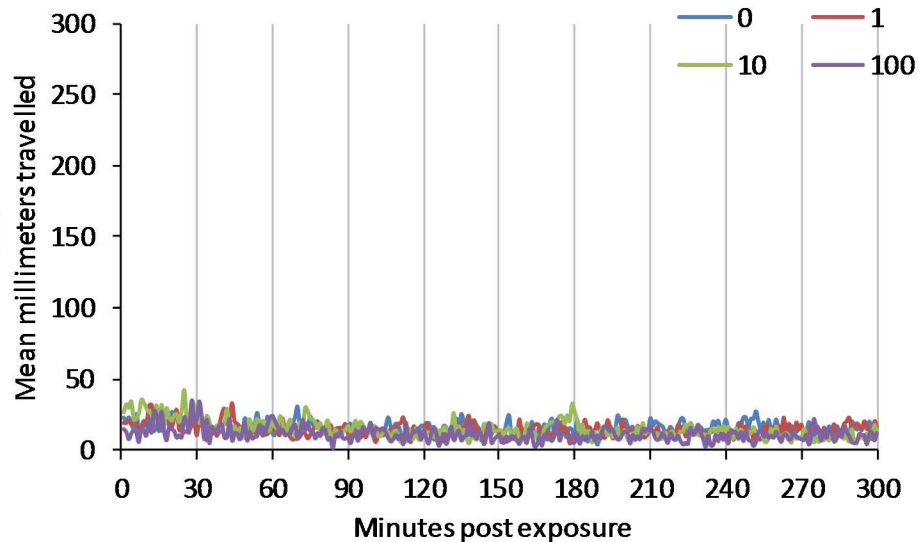
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.046	0.926	0.957	1.000	0.763	0.819	0.926	0.504	0.473	1.000
10	0.763	0.741	0.042	0.944	0.521	0.471	0.882	0.161	0.130	0.270
100	1.000	0.154	0.786	0.632	0.482	0.745	0.999	0.668	0.199	1.000
1000	1.000	0.332	0.010	0.843	0.011	0.277	0.618	0.439	0.083	0.394

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Muscimol



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 93	100 ± 103	100 ± 88	100 ± 107	100 ± 88	100 ± 96	100 ± 93	100 ± 95	100 ± 98	100 ± 99	24
1	98 ± 81	100 ± 95	80 ± 96	88 ± 94	96 ± 89	90 ± 90	93 ± 90	79 ± 84	84 ± 77	102 ± 95	24
10	137 ± 77	108 ± 92	99 ± 84	86 ± 79	89 ± 78	116 ± 172	88 ± 79	76 ± 86	66 ± 70	63 ± 52	24
100	79 ± 41	87 ± 36	73 ± 61	79 ± 64	70 ± 52	61 ± 60	76 ± 65	54 ± 46	57 ± 41	70 ± 63	23

## Mean ± standard deviation

‡ Exclusion: lethality observed in 1000 μM treatment group (24 of 24 animals)

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	62-138	58-142	64-136	56-144	64-136	61-139	62-138	61-139	60-140	60-140
1	65-132	61-138	40-119	49-126	60-133	54-127	56-130	45-113	53-115	64-141
10	105-168	71-146	64-133	54-119	57-121	46-186	56-120	41-111	38-95	41-84
100	61-96	72-102	47-98	52-105	49-92	36-86	49-103	34-73	39-74	44-96

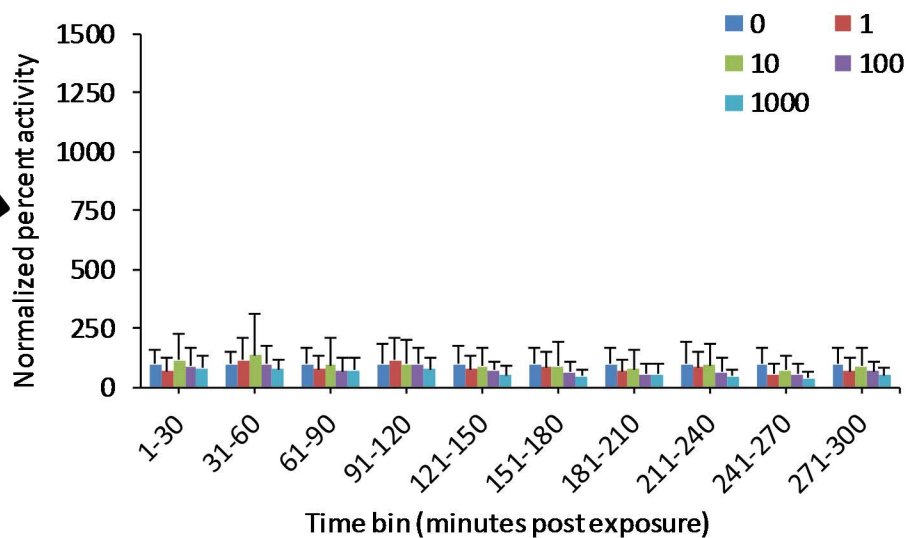
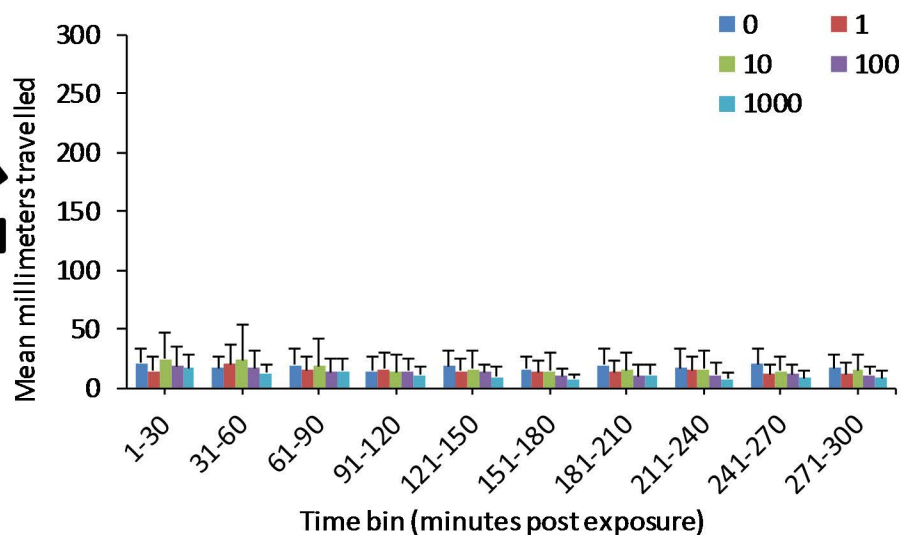
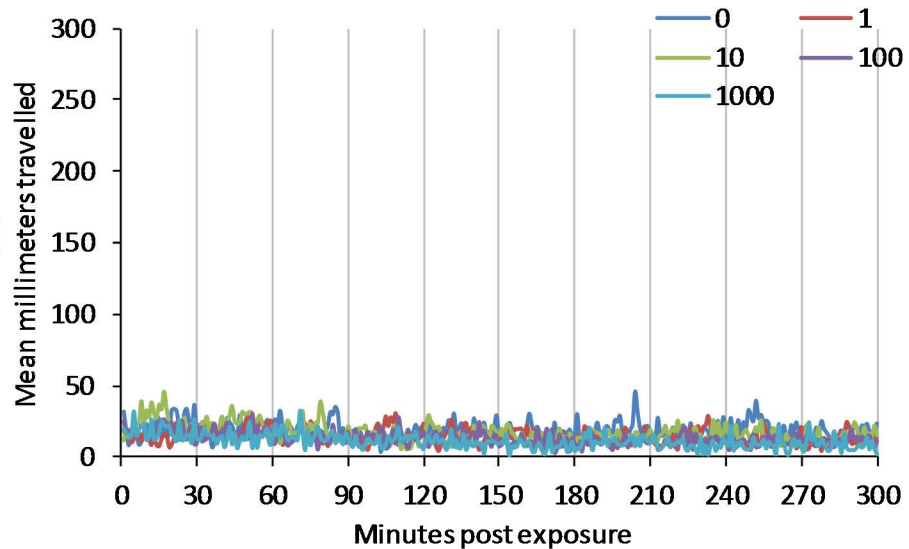
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.999	0.998	0.568	0.979	0.992	1.000	1.000	0.908	0.986	1.000
10	0.116	0.692	0.998	0.996	1.000	0.998	0.999	0.900	0.766	0.830
100	1.000	0.842	0.902	1.000	0.893	0.565	0.970	0.548	0.788	0.933

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

**CHEMICAL: SKF 97541 (CGP 35024)**



**Normalized percent activity**

	Time bin (minutes post exposure)										
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 56	100 $\pm$ 52	100 $\pm$ 67	100 $\pm$ 83	100 $\pm$ 75	100 $\pm$ 70	100 $\pm$ 70	100 $\pm$ 91	100 $\pm$ 66	100 $\pm$ 65	16
1	67 $\pm$ 62	117 $\pm$ 94	76 $\pm$ 56	115 $\pm$ 97	75 $\pm$ 61	85 $\pm$ 66	69 $\pm$ 47	86 $\pm$ 65	58 $\pm$ 41	69 $\pm$ 57	15
10	115 $\pm$ 111	136 $\pm$ 179	94 $\pm$ 115	97 $\pm$ 102	88 $\pm$ 84	90 $\pm$ 102	78 $\pm$ 81	94 $\pm$ 90	71 $\pm$ 63	89 $\pm$ 80	14
100	90 $\pm$ 80	98 $\pm$ 81	68 $\pm$ 59	99 $\pm$ 73	71 $\pm$ 39	66 $\pm$ 38	55 $\pm$ 45	65 $\pm$ 63	56 $\pm$ 44	68 $\pm$ 42	16
1000	82 $\pm$ 55	76 $\pm$ 42	74 $\pm$ 50	76 $\pm$ 54	52 $\pm$ 44	47 $\pm$ 30	55 $\pm$ 46	46 $\pm$ 28	41 $\pm$ 29	50 $\pm$ 34	16

**Mean  $\pm$  standard deviation**

**Normalized percent activity**

	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	72-128	74-126	67-133	58-142	62-138	65-135	65-135	54-146	67-133	67-133
1	35-99	68-165	47-105	65-165	44-107	51-119	45-94	52-119	37-79	40-99
10	56-174	41-232	33-166	42-151	43-133	35-144	35-122	46-142	37-105	46-131
100	50-131	57-138	39-98	63-136	52-91	47-86	32-77	34-96	34-78	47-89
1000	54-110	54-97	49-99	49-103	30-74	32-62	32-79	32-60	27-55	33-68

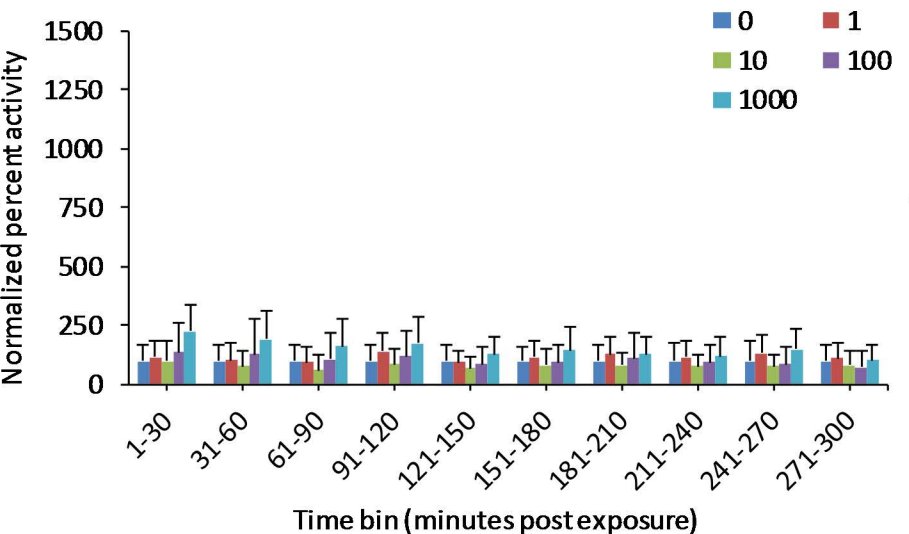
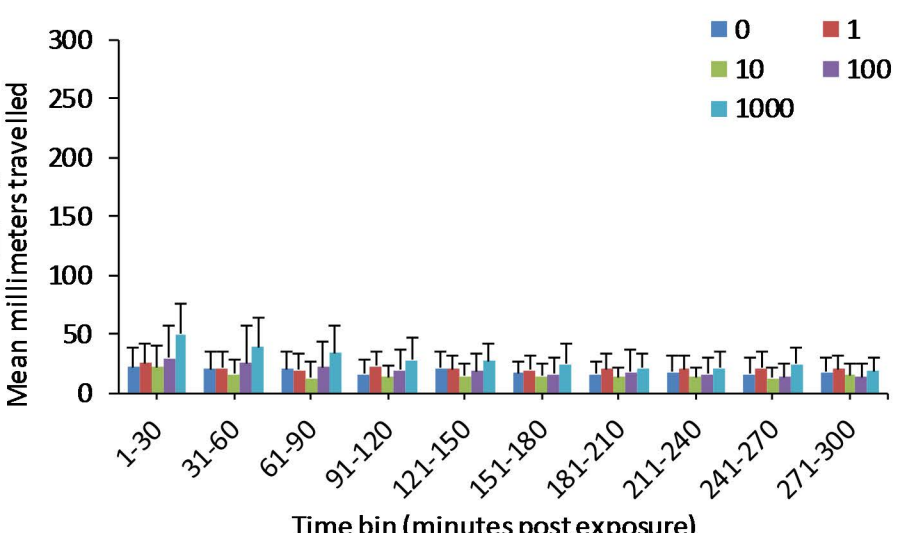
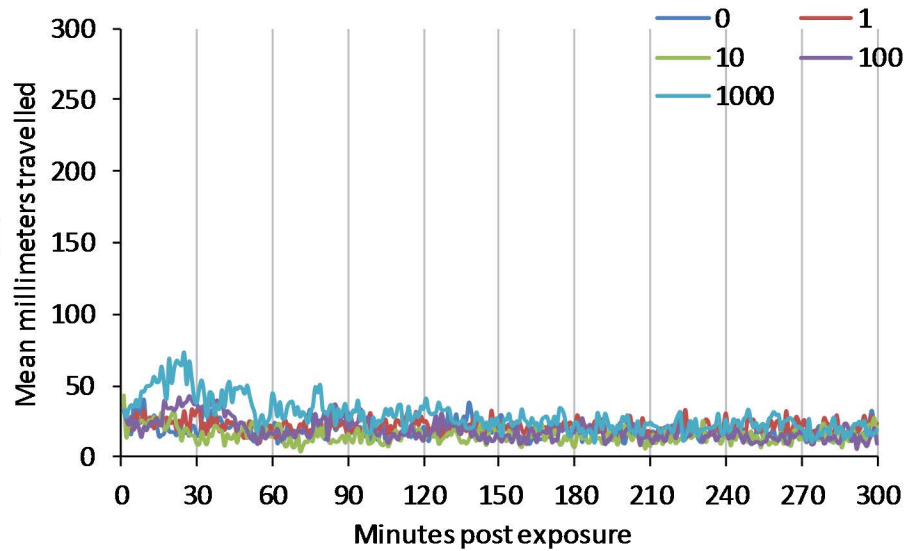
**95% confidence interval**

**p-values**

	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.296	1.000	0.795	0.994	0.840	0.992	0.795	1.000	0.251	0.591
10	0.962	1.000	0.722	0.985	0.945	0.856	0.522	1.000	0.649	0.970
100	0.817	0.991	0.508	1.000	0.961	0.862	0.172	0.708	0.226	0.791
1000	0.918	0.859	0.788	0.929	0.250	0.291	0.191	0.605	0.036	0.246

**Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$**

# CHEMICAL: Valproic Acid



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 71	100 ± 71	100 ± 71	100 ± 72	100 ± 65	100 ± 60	100 ± 68	100 ± 77	100 ± 85	100 ± 70	19
1	115 ± 70	102 ± 71	96 ± 65	141 ± 79	95 ± 52	117 ± 70	127 ± 78	114 ± 71	130 ± 82	111 ± 65	22
10	97 ± 86	78 ± 63	61 ± 65	85 ± 63	68 ± 52	83 ± 68	81 ± 57	79 ± 49	78 ± 52	83 ± 57	20
100	135 ± 123	126 ± 151	105 ± 110	119 ± 113	88 ± 71	92 ± 80	110 ± 112	92 ± 77	84 ± 72	74 ± 65	23
1000	224 ± 113	190 ± 123	162 ± 117	173 ± 115	128 ± 73	145 ± 101	129 ± 75	119 ± 82	149 ± 86	102 ± 65	21

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	67-133	67-133	68-132	67-133	70-130	72-128	69-131	64-136	61-139	68-132
1	85-145	72-132	68-123	107-175	73-117	87-147	94-160	84-145	95-165	83-139
10	59-136	49-106	32-91	57-113	44-91	52-113	56-106	57-100	54-101	57-108
100	83-186	63-189	60-151	72-166	58-117	59-126	63-157	60-125	54-114	47-101
1000	175-274	137-244	111-213	123-223	96-160	101-189	96-162	83-155	111-187	74-131

## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.942	1.000	1.000	0.498	1.000	0.951	0.861	0.924	0.671	0.956
10	1.000	0.831	0.284	0.997	0.647	0.961	0.947	0.997	0.987	0.981
100	0.942	0.996	0.990	0.999	0.936	0.965	1.000	1.000	0.971	0.825
1000	0.001	0.023	0.299	0.171	0.799	0.794	0.787	0.858	0.363	0.998

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# GABA antagonists and negative modulators

**6 tested chemicals:**

Bicuculline

Dehydroisoandrosterone 3-sulfate sodium

Pentylentetrazol

Picrotoxin

Pregnenolone sulfate sodium

SCH 50911

# CHEMICAL: Bicuculline

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 90	100 $\pm$ 109	100 $\pm$ 97	100 $\pm$ 98	100 $\pm$ 110	100 $\pm$ 99	100 $\pm$ 119	100 $\pm$ 122	100 $\pm$ 135	100 $\pm$ 90	24
1	139 $\pm$ 85	145 $\pm$ 106	120 $\pm$ 89	131 $\pm$ 106	146 $\pm$ 123	111 $\pm$ 100	153 $\pm$ 110	140 $\pm$ 109	154 $\pm$ 131	134 $\pm$ 97	23
10	814 $\pm$ 177	966 $\pm$ 108	732 $\pm$ 91	780 $\pm$ 132	767 $\pm$ 113	690 $\pm$ 104	861 $\pm$ 153	818 $\pm$ 170	945 $\pm$ 189	708 $\pm$ 116	23
100	335 $\pm$ 63	430 $\pm$ 85	500 $\pm$ 70	599 $\pm$ 93	517 $\pm$ 114	422 $\pm$ 86	541 $\pm$ 93	543 $\pm$ 80	666 $\pm$ 100	554 $\pm$ 85	23

## Mean $\pm$ standard deviation

<sup>‡</sup>Exclusion: lethality observed in 1000  $\mu$ M treatment group (24 of 24 animals)

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	63-137	56-144	60-140	60-140	55-145	60-140	51-149	50-150	45-155	63-137
1	103-174	101-190	83-157	87-175	95-198	70-153	107-199	95-185	100-209	94-175
10	740-888	921-1011	694-770	725-835	720-814	647-733	797-925	747-889	866-1024	659-756
100	309-362	394-465	471-529	560-638	469-564	386-458	502-580	509-576	624-708	519-589

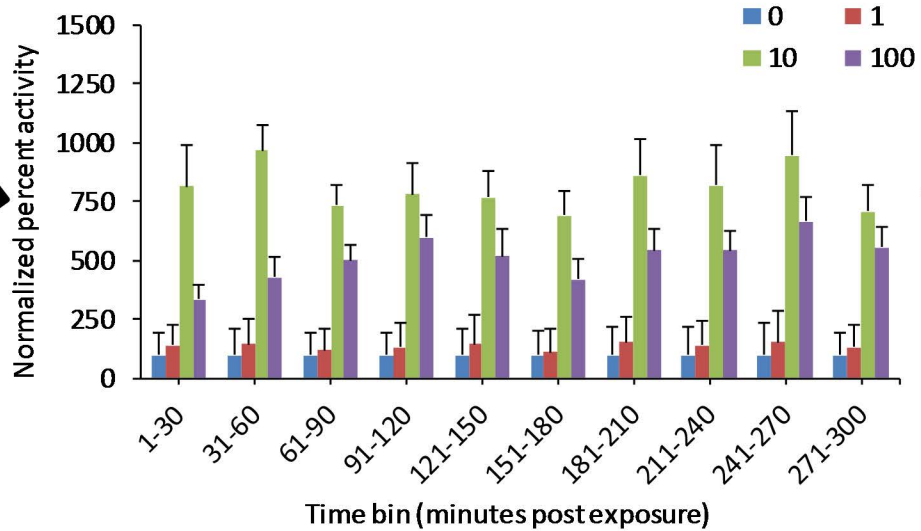
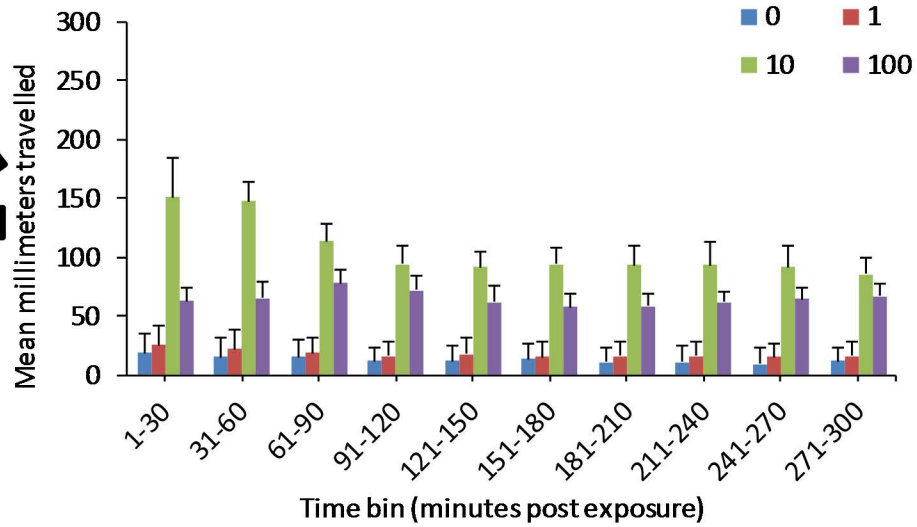
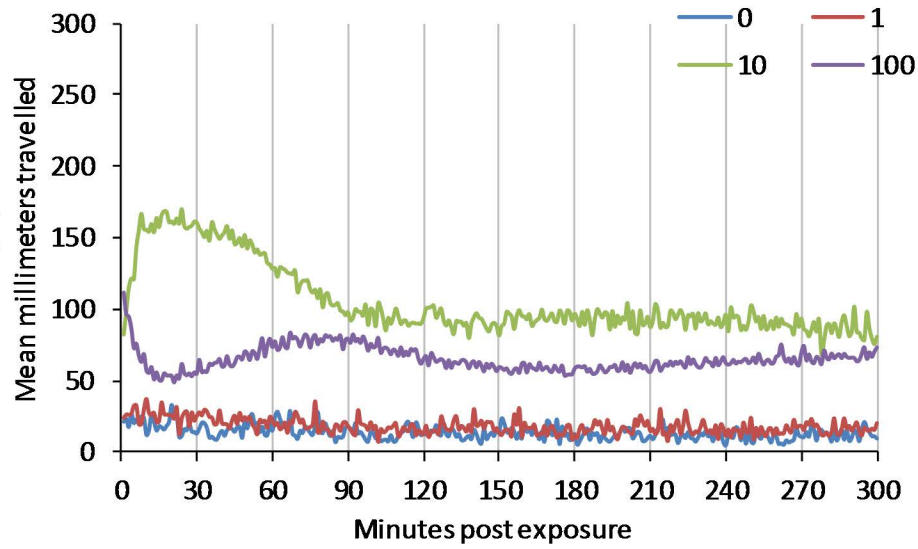
## 95% confidence interval

## p-values

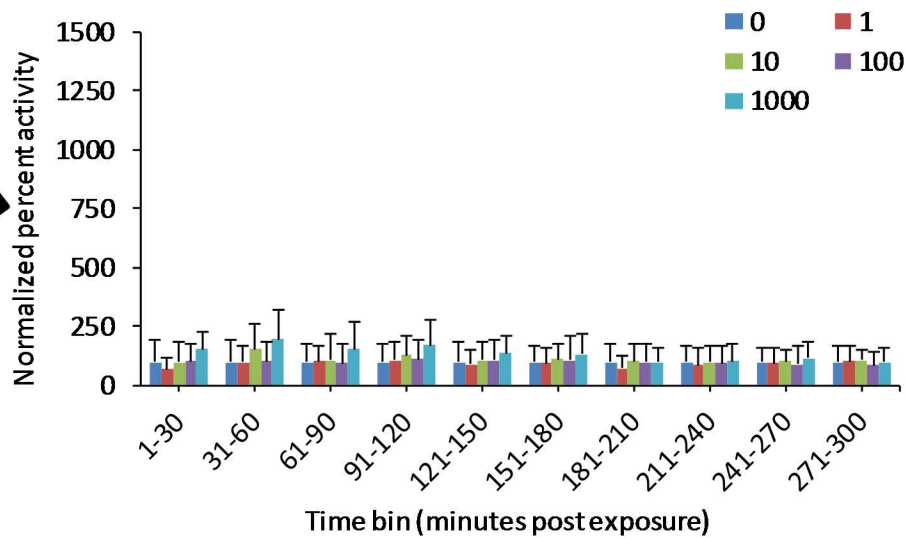
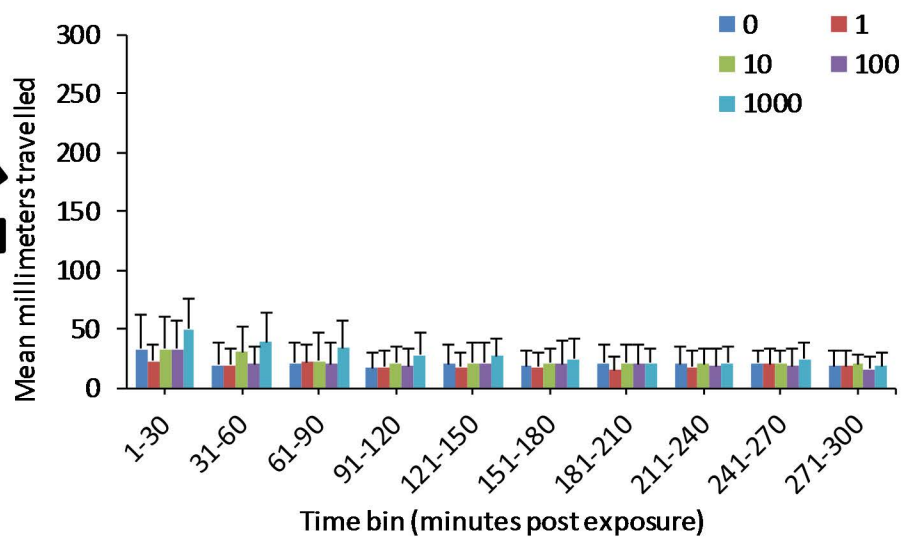
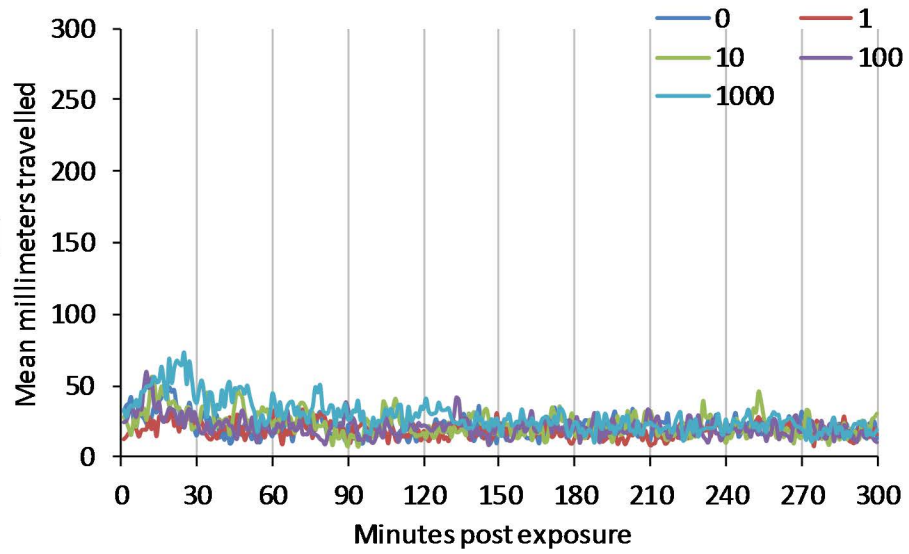
## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.193	0.077	0.618	0.545	0.227	0.980	0.070	0.206	0.102	0.475
10	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
100	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Dehydroisoandrosterone 3-sulfate sodium



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 90	100 ± 95	100 ± 79	100 ± 78	100 ± 85	100 ± 71	100 ± 73	100 ± 71	100 ± 56	100 ± 68	24
1	69 ± 45	97 ± 74	101 ± 69	106 ± 80	88 ± 59	94 ± 65	72 ± 55	87 ± 71	96 ± 62	101 ± 67	23
10	100 ± 85	152 ± 107	107 ± 113	128 ± 79	106 ± 82	111 ± 63	102 ± 71	100 ± 68	101 ± 52	107 ± 48	21
100	101 ± 75	104 ± 78	95 ± 82	110 ± 88	106 ± 86	107 ± 104	98 ± 78	93 ± 72	90 ± 74	88 ± 58	22
1000	153 ± 77	197 ± 127	156 ± 112	169 ± 112	135 ± 77	130 ± 91	99 ± 58	103 ± 71	116 ± 67	99 ± 63	21

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	63-137	61-139	68-132	68-132	65-135	71-129	70-130	71-129	77-123	72-128
1	50-88	66-128	72-130	73-140	63-113	67-121	49-95	57-117	70-122	73-130
10	63-137	106-199	57-156	94-162	70-142	84-139	71-133	70-129	78-124	87-128
100	69-133	70-137	60-130	72-147	70-143	63-151	65-132	62-124	58-121	63-112
1000	119-186	141-252	107-204	120-218	102-168	91-170	74-125	72-134	87-145	72-127

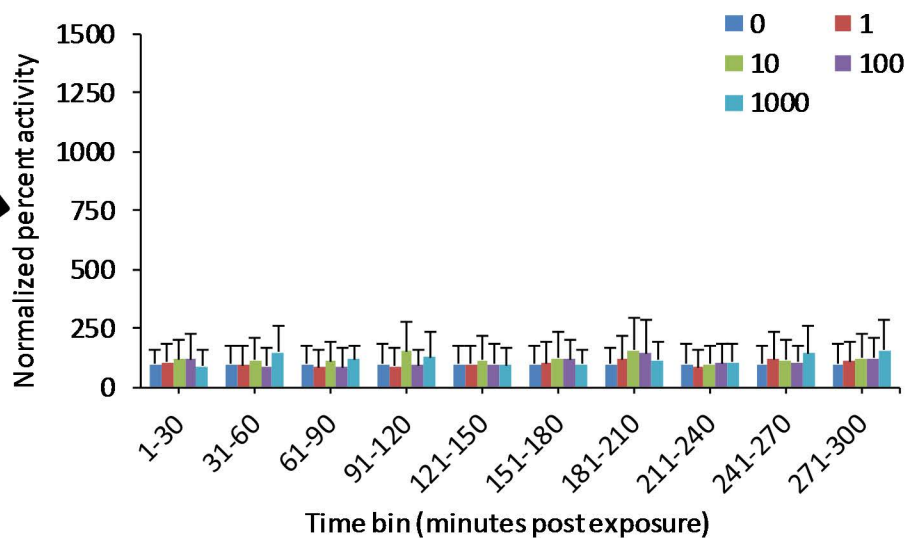
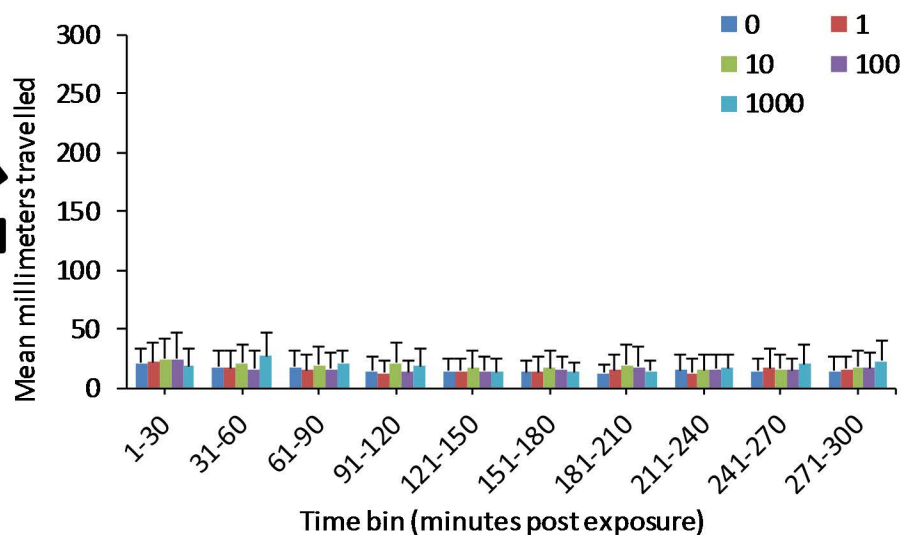
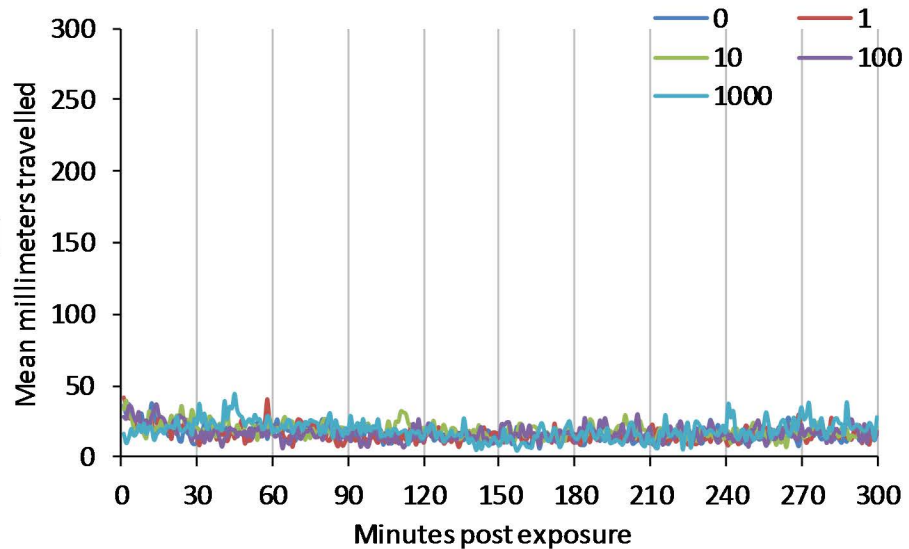
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.623	0.998	0.999	1.000	1.000	1.000	0.617	0.991	0.994	1.000
10	1.000	0.170	0.996	0.841	0.986	0.913	0.999	0.999	1.000	0.959
100	0.999	1.000	0.999	1.000	0.997	1.000	0.999	0.992	0.871	0.984
1000	0.106	0.002	0.241	0.216	0.332	0.930	0.999	1.000	0.996	1.000

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Pentylene tetrazole



## Normalized percent activity

[ $\mu\text{M}$ ]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 59	100 ± 74	100 ± 79	100 ± 84	100 ± 74	100 ± 73	100 ± 66	100 ± 82	100 ± 73	100 ± 82	24
1	106 ± 81	95 ± 79	86 ± 70	91 ± 79	100 ± 76	103 ± 90	119 ± 103	84 ± 75	120 ± 116	111 ± 79	24
10	118 ± 83	116 ± 92	110 ± 85	152 ± 126	117 ± 105	124 ± 110	157 ± 135	99 ± 82	115 ± 88	124 ± 103	24
100	118 ± 108	90 ± 82	87 ± 77	96 ± 68	98 ± 83	119 ± 79	144 ± 142	104 ± 78	109 ± 71	122 ± 89	23
1000	90 ± 70	149 ± 112	118 ± 62	130 ± 106	94 ± 75	97 ± 61	115 ± 78	108 ± 81	144 ± 119	159 ± 130	24

## Mean ± standard deviation

## Normalized percent activity

[ $\mu\text{M}$ ]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	76-124	70-130	68-132	66-134	70-130	70-130	73-127	67-133	70-130	67-133
1	72-139	62-127	58-115	59-123	69-131	66-140	78-161	54-115	73-168	79-144
10	84-152	78-153	75-145	100-203	74-159	79-169	102-212	66-132	80-151	82-166
100	73-163	56-124	55-119	68-124	64-133	86-152	85-203	72-137	79-138	85-159
1000	61-119	103-194	92-143	86-173	63-124	73-122	83-147	75-141	95-193	105-212

## 95% confidence interval

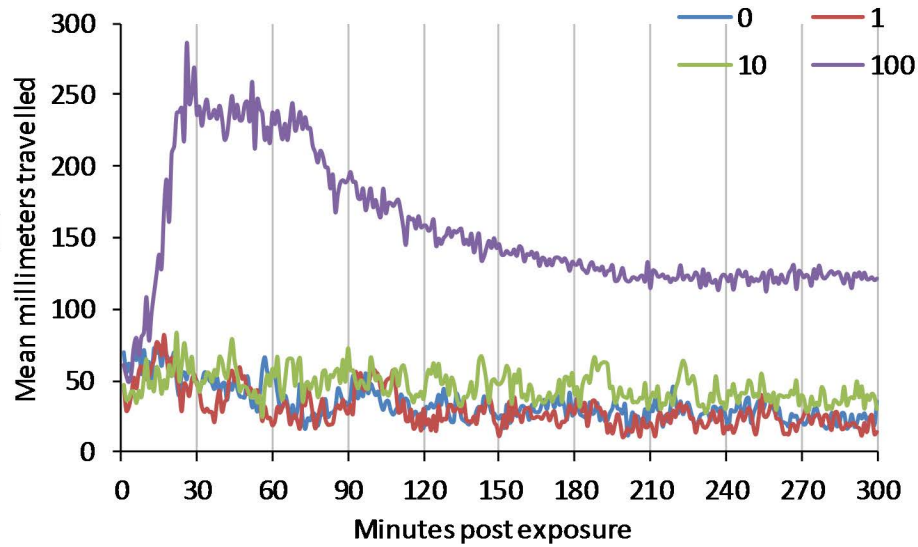
## p-values

[ $\mu\text{M}$ ]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	1.000	0.982	0.947	0.994	1.000	1.000	0.998	0.978	1.000	0.985
10	0.995	0.997	0.998	0.464	1.000	0.961	0.632	1.000	0.997	0.955
100	1.000	0.963	0.972	1.000	0.999	0.947	0.980	0.996	1.000	0.896
1000	0.878	0.554	0.844	0.839	0.997	1.000	0.996	0.995	0.833	0.319

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



**CHEMICAL: Picrotoxin**



**Normalized percent activity**

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 60	100 ± 65	100 ± 54	100 ± 59	100 ± 71	100 ± 65	100 ± 68	100 ± 54	100 ± 70	100 ± 65	24
1	87 ± 48	81 ± 47	90 ± 56	111 ± 76	87 ± 62	84 ± 48	86 ± 46	81 ± 66	79 ± 59	91 ± 64	23
10	84 ± 50	107 ± 64	169 ± 90	134 ± 79	162 ± 95	145 ± 80	171 ± 69	143 ± 64	144 ± 103	158 ± 91	22
100	248 ± 51	504 ± 137	683 ± 204	478 ± 116	502 ± 126	449 ± 116	473 ± 97	429 ± 76	432 ± 86	536 ± 118	21

Mean ± standard deviation

‡ Exclusion: lethality observed in 1000  $\mu\text{M}$  treatment group (22 of 22 animals)

**Normalized percent activity**

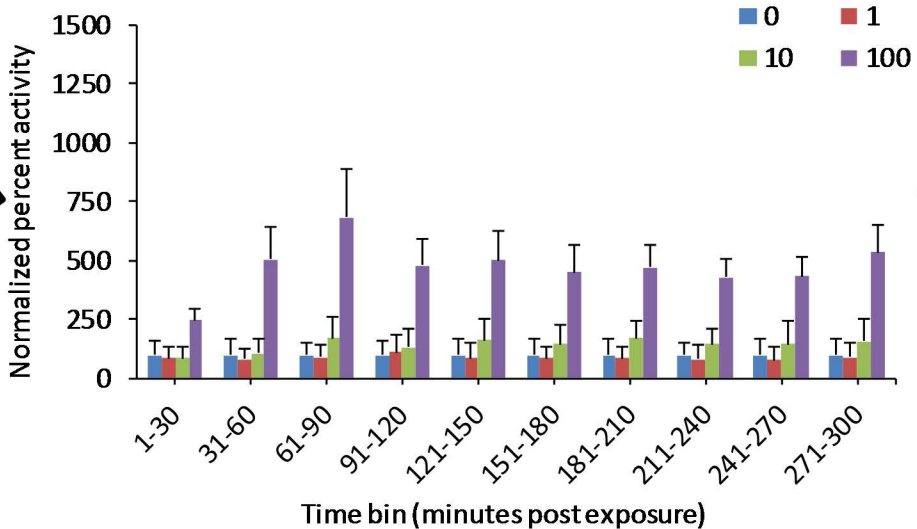
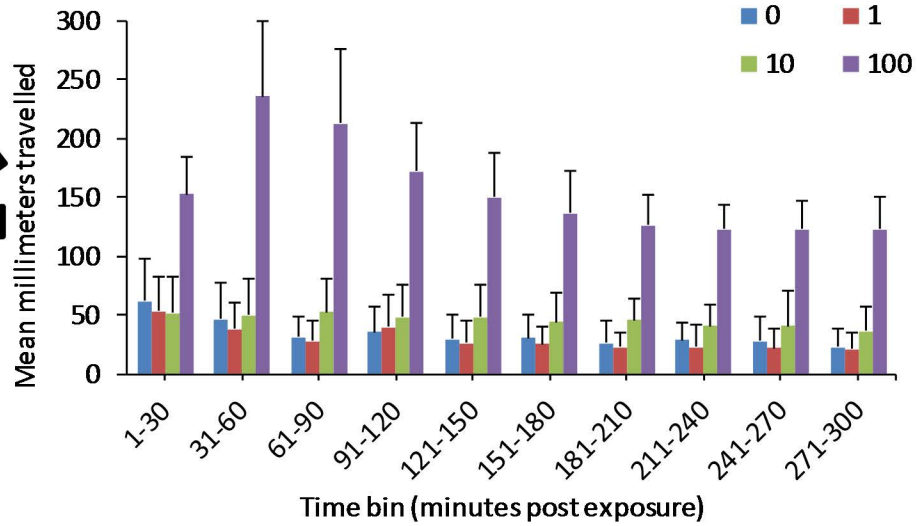
	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	76-124	74-126	78-122	76-124	71-129	74-126	72-128	78-122	71-129	73-127
1	67-107	62-101	67-113	79-143	61-113	64-104	67-105	53-108	54-104	64-118
10	62-105	80-135	130-207	100-167	121-202	110-179	142-201	116-171	100-188	120-197
100	225-270	445-564	594-772	428-529	447-557	399-500	431-515	395-462	395-470	484-587

95% confidence interval

**p-values**

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.831	0.699	0.935	0.992	0.902	0.830	0.902	0.265	0.276	0.897
10	0.661	0.982	0.025	0.227	0.012	0.148	0.004	0.156	0.585	0.062
100	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Pregnenolone sulfate sodium

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 81	100 $\pm$ 90	100 $\pm$ 66	100 $\pm$ 75	100 $\pm$ 74	100 $\pm$ 96	100 $\pm$ 76	100 $\pm$ 66	100 $\pm$ 74	100 $\pm$ 73	24
1	81 $\pm$ 71	91 $\pm$ 88	112 $\pm$ 99	116 $\pm$ 91	105 $\pm$ 89	108 $\pm$ 77	100 $\pm$ 71	122 $\pm$ 80	109 $\pm$ 85	113 $\pm$ 73	20
10	95 $\pm$ 53	174 $\pm$ 146	138 $\pm$ 144	154 $\pm$ 100	150 $\pm$ 114	132 $\pm$ 88	134 $\pm$ 87	153 $\pm$ 100	151 $\pm$ 129	152 $\pm$ 98	24
100	134 $\pm$ 83	131 $\pm$ 98	147 $\pm$ 120	136 $\pm$ 116	118 $\pm$ 95	138 $\pm$ 106	140 $\pm$ 80	163 $\pm$ 98	158 $\pm$ 94	133 $\pm$ 78	22
1000	161 $\pm$ 106	225 $\pm$ 222	207 $\pm$ 213	167 $\pm$ 225	120 $\pm$ 128	117 $\pm$ 99	99 $\pm$ 92	131 $\pm$ 109	133 $\pm$ 100	131 $\pm$ 97	24

## Mean $\pm$ standard deviation

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	67-133	63-137	73-127	69-131	70-130	61-139	69-131	73-127	70-130	70-130
1	50-113	52-130	68-157	75-157	65-144	74-143	68-131	86-158	71-147	80-146
10	74-117	114-233	129-247	113-195	104-197	96-168	99-170	113-194	98-203	112-192
100	99-170	90-173	95-198	86-186	78-159	92-183	106-174	122-205	118-198	100-167
1000	118-204	135-315	120-294	76-259	67-172	76-158	62-137	87-176	92-174	91-170

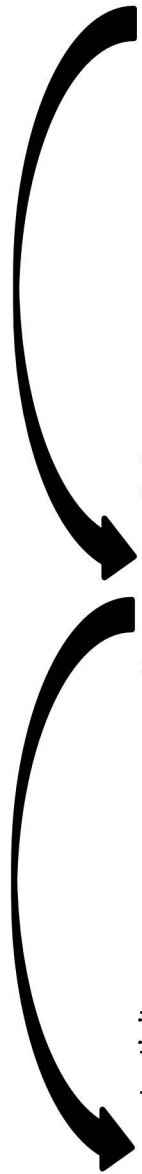
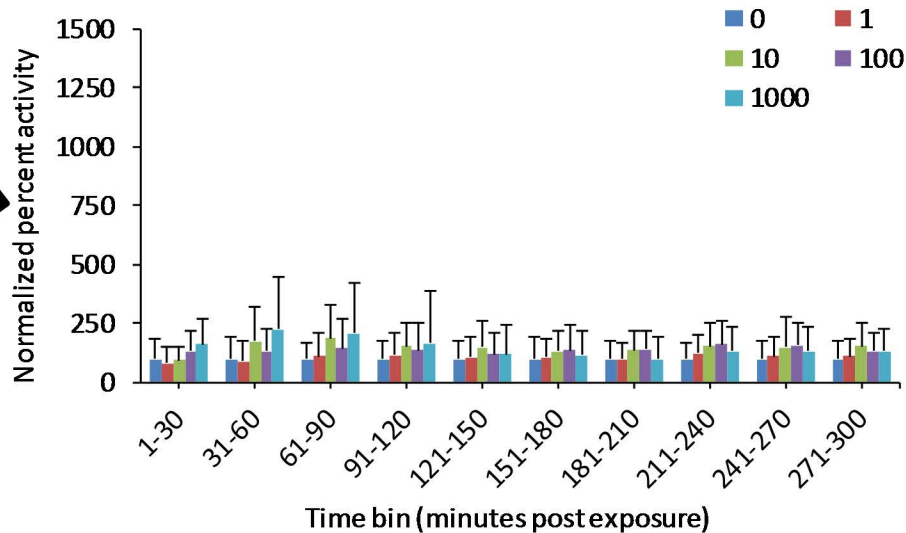
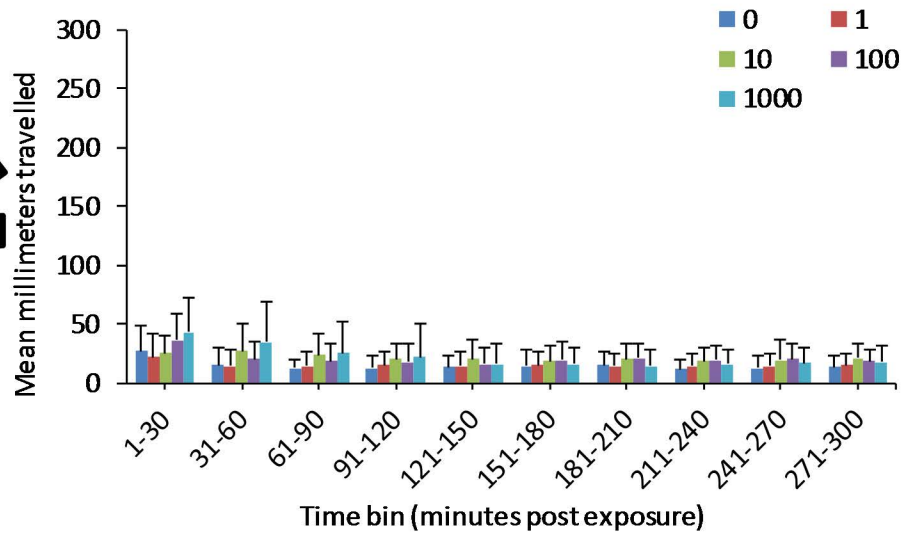
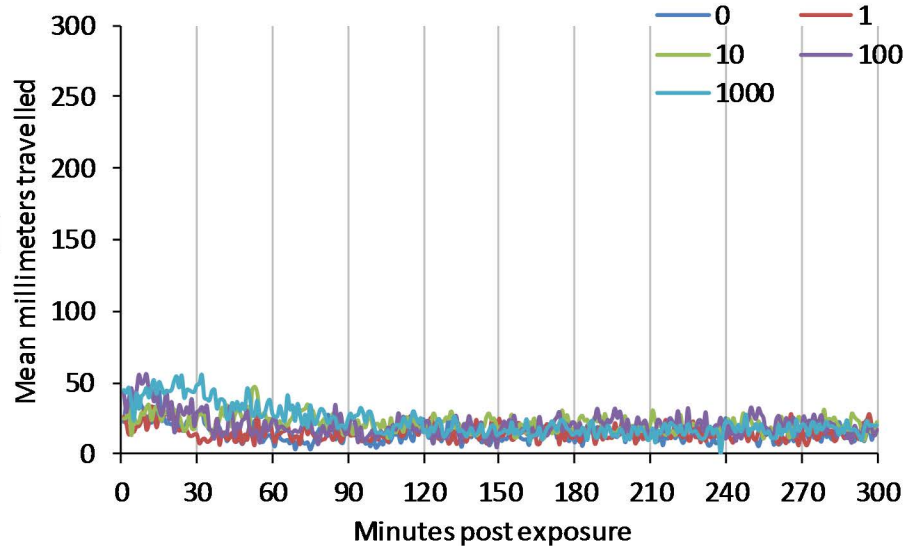
## 95% confidence interval

## p-values

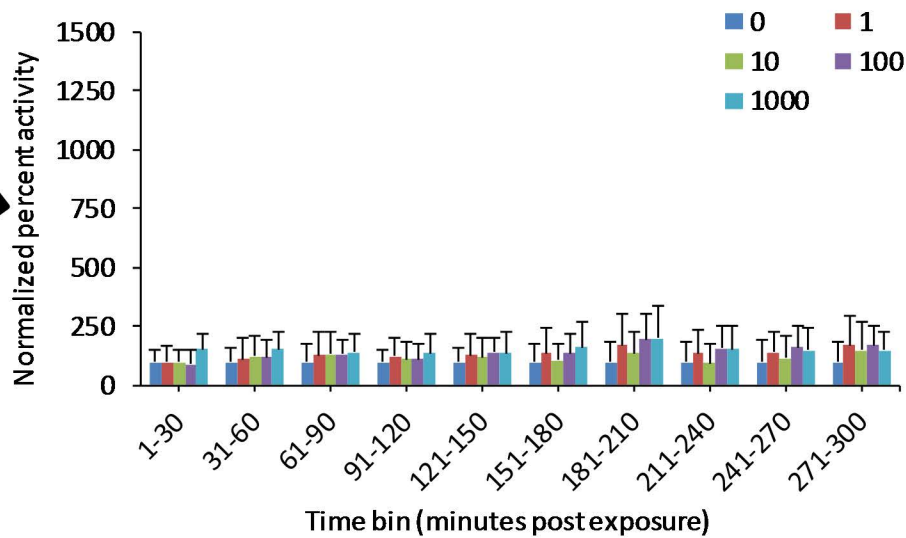
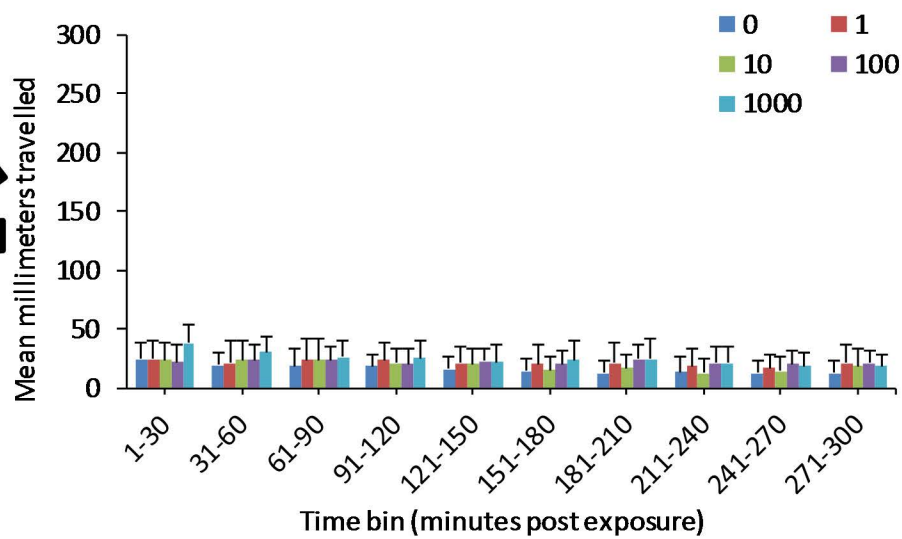
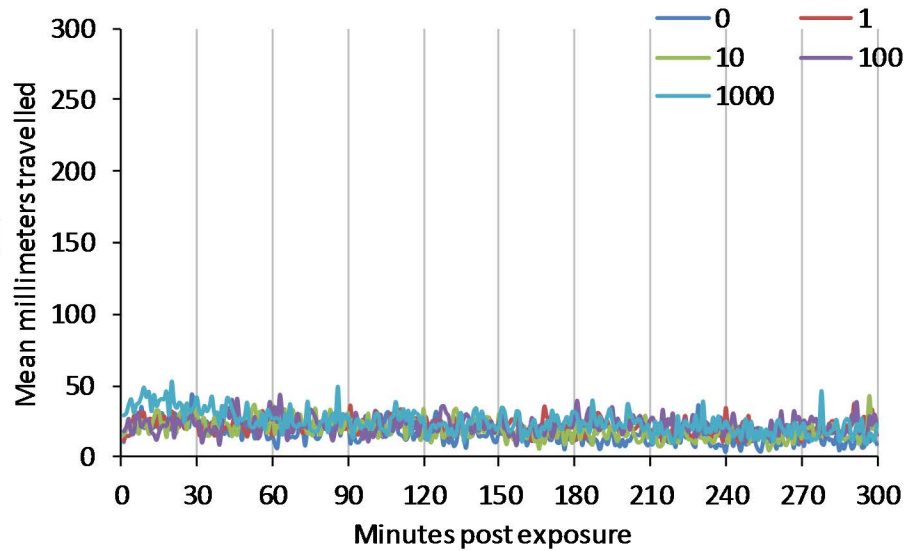
## Time bin (minutes post exposure)

[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.686	0.979	1.000	0.996	1.000	0.965	1.000	0.981	1.000	0.973
10	0.996	0.206	0.147	0.386	0.628	0.576	0.823	0.666	0.579	0.370
100	0.381	0.720	0.779	0.879	0.974	0.645	0.554	0.358	0.353	0.634
1000	0.079	0.013	0.337	0.915	1.000	0.989	0.978	0.997	0.936	0.875

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: SCH 50911



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 54	100 ± 58	100 ± 78	100 ± 52	100 ± 64	100 ± 75	100 ± 82	100 ± 87	100 ± 93	100 ± 82	16
1	100 ± 65	110 ± 93	129 ± 102	125 ± 78	130 ± 85	138 ± 110	172 ± 134	135 ± 102	139 ± 91	172 ± 127	16
10	97 ± 58	124 ± 87	131 ± 93	112 ± 71	122 ± 77	107 ± 74	138 ± 90	95 ± 81	117 ± 94	149 ± 117	16
100	90 ± 59	120 ± 70	131 ± 62	111 ± 65	139 ± 67	138 ± 78	198 ± 102	156 ± 95	164 ± 85	169 ± 85	14
1000	154 ± 66	155 ± 68	141 ± 80	136 ± 84	135 ± 88	163 ± 105	198 ± 139	151 ± 100	149 ± 97	150 ± 78	14

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	73-127	71-129	61-139	74-126	68-132	62-138	59-141	56-144	54-146	59-141
1	68-133	64-157	78-180	86-164	87-173	83-193	104-239	84-186	93-184	109-235
10	68-126	81-168	84-177	77-148	83-160	70-143	93-182	55-135	70-164	90-208
100	58-121	83-157	97-164	76-146	103-175	96-179	143-252	105-207	118-209	123-214
1000	119-189	119-192	99-184	92-181	88-182	107-219	124-272	98-205	97-200	108-191

## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	1.000	1.000	0.893	0.955	0.855	0.879	0.444	0.873	0.693	0.361
10	0.998	0.978	0.811	0.999	0.950	0.998	0.806	1.000	0.983	0.721
100	0.961	0.954	0.629	0.996	0.614	0.660	0.095	0.452	0.311	0.306
1000	0.209	0.289	0.449	0.796	0.789	0.294	0.098	0.487	0.522	0.562

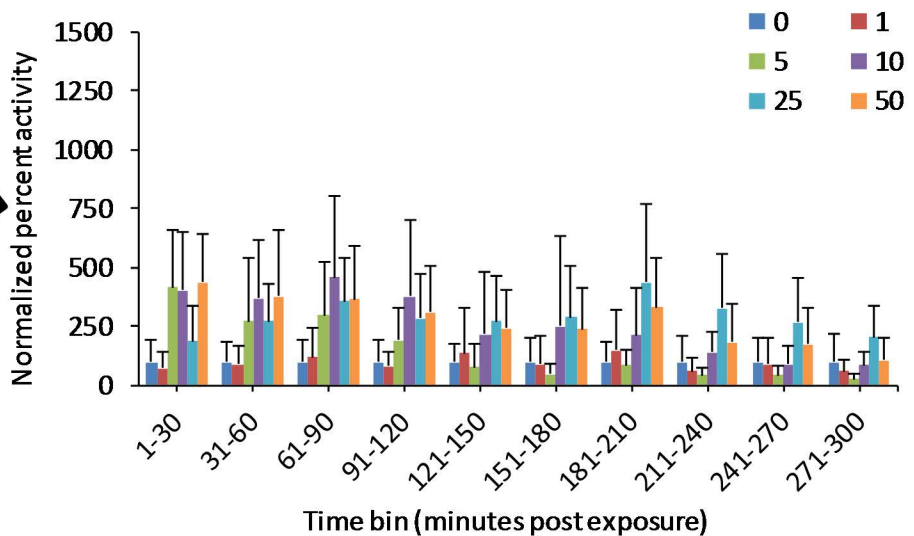
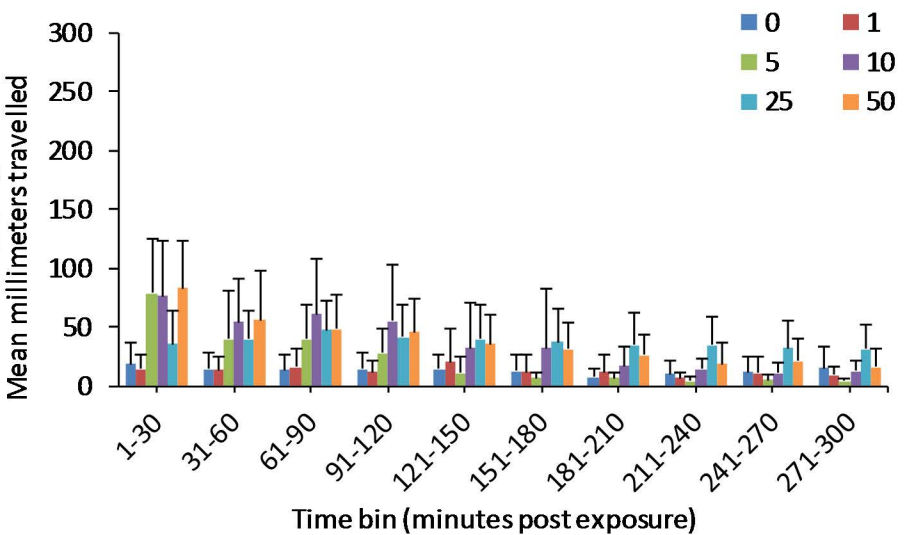
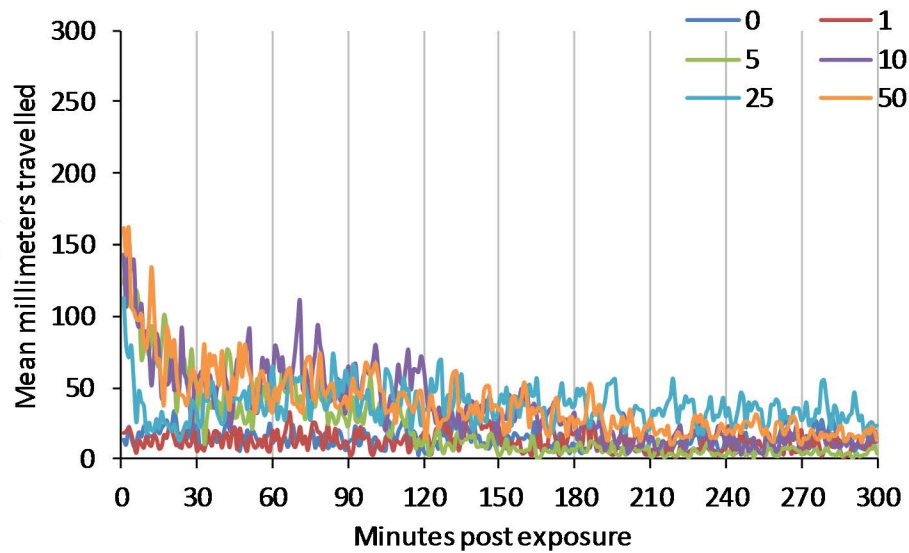
Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# Flavonoids and flavonoid-like compounds

## 24 tested chemicals:

3'-Hydroxyflavone  
6-Hydroxyflavone  
7-Hydroxyflavone  
 $\alpha$ -Naphthoflavone  
 $\beta$ -Naphthoflavone  
Apigenin  
Biochanin A  
Chrysin  
Daidzein  
(S)-Equol  
Fisetin  
Flavone  
Formononetin  
Galangin  
Genistein  
Kaempferol  
Luteolin  
Morin  
Myricetin  
Naringenin  
Puerarin  
Quercetin  
Quercetin 3- $\beta$ -D glucoside  
Resveratrol

# CHEMICAL: 3'-Hydroxyflavone



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 90	100 ± 87	100 ± 96	100 ± 90	100 ± 79	100 ± 101	100 ± 85	100 ± 111	100 ± 100	100 ± 116	16
1	74 ± 68	89 ± 77	19 ± 23	82 ± 63	137 ± 189	89 ± 123	147 ± 174	62 ± 55	90 ± 114	60 ± 51	16
5	414 ± 248	271 ± 271	299 ± 226	193 ± 138	77 ± 96	50 ± 43	86 ± 65	42 ± 33	44 ± 37	28 ± 18	16
10	404 ± 248	368 ± 250	459 ± 348	376 ± 329	215 ± 264	252 ± 382	213 ± 200	139 ± 85	90 ± 78	85 ± 61	16
25	186 ± 153	271 ± 162	358 ± 184	285 ± 185	270 ± 192	291 ± 213	437 ± 331	328 ± 231	267 ± 194	203 ± 135	16
50	436 ± 210	377 ± 285	364 ± 225	311 ± 194	242 ± 164	240 ± 171	330 ± 209	182 ± 162	174 ± 156	106 ± 99	16

Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	55-145	57-143	52-148	55-145	61-139	50-150	57-143	45-155	50-150	42-158
1	40-108	51-128	58-181	50-113	43-231	27-150	60-235	34-89	33-147	35-86
5	291-538	135-407	186-412	124-262	29-125	28-71	54-119	26-59	25-62	19-37
10	279-528	244-493	285-634	212-541	83-347	61-443	113-313	96-182	51-128	55-116
25	109-262	190-352	266-450	192-377	174-366	185-397	271-602	212-444	170-364	135-271
50	332-541	234-519	252-476	214-408	161-324	154-325	225-434	101-263	96-252	57-166

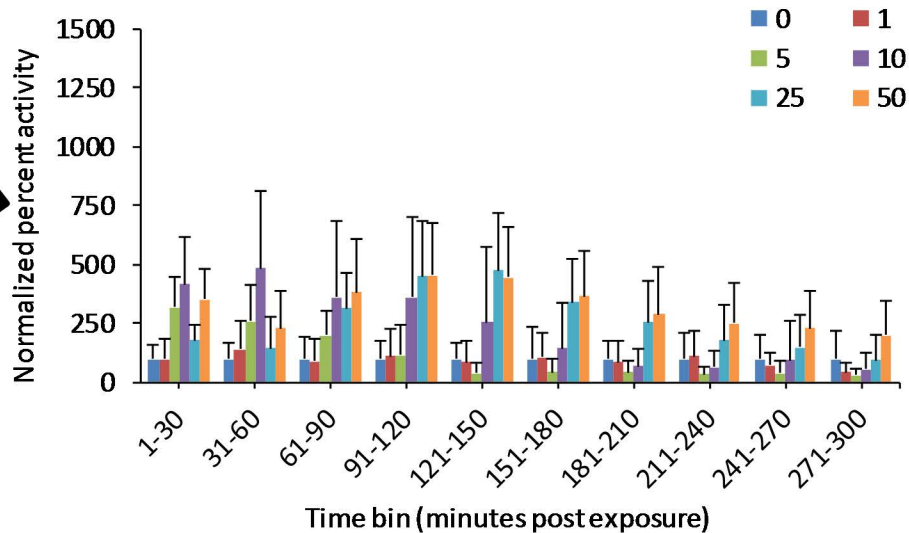
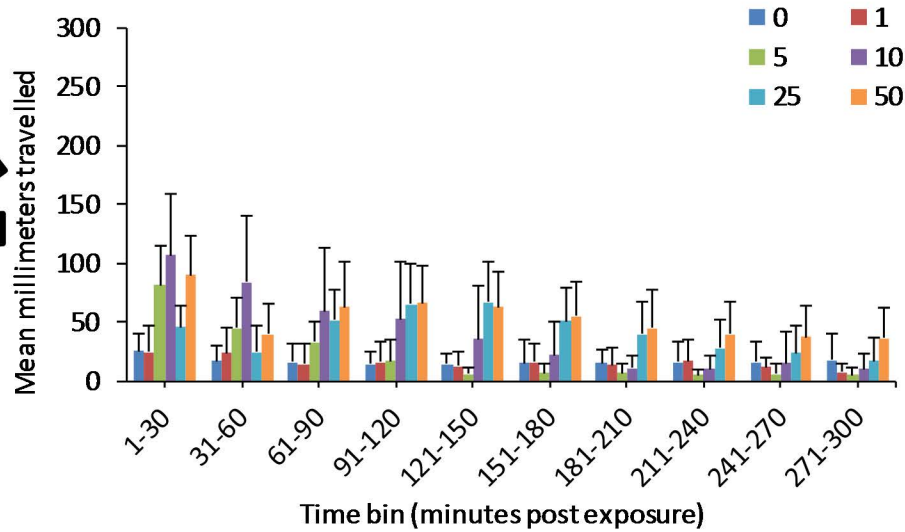
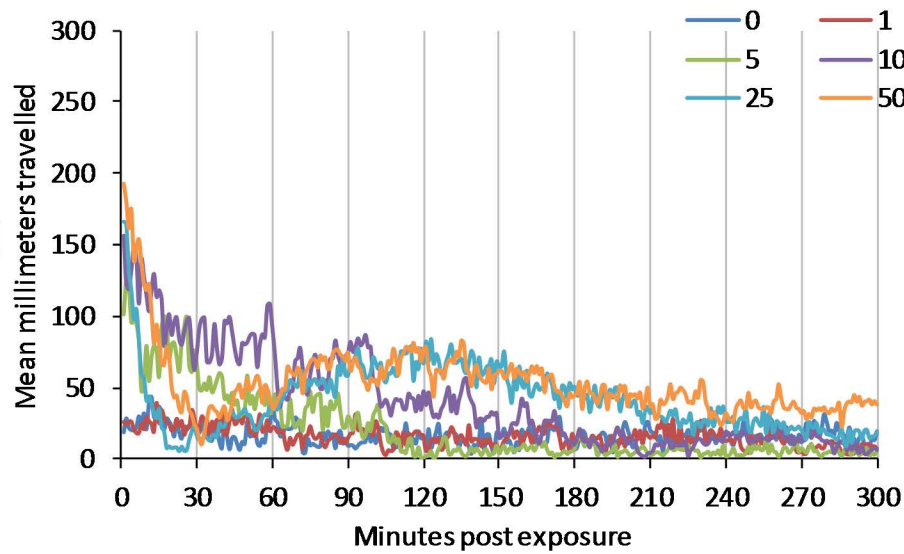
95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.959	1.000	0.999	1.000	1.000	0.995	0.939	0.995	0.998	0.975
5	0.001	0.035	0.002	0.217	0.739	0.814	1.000	0.801	0.425	0.167
10	0.001	0.001	0.001	0.001	0.420	0.050	0.169	0.231	1.000	0.998
25	0.122	0.001	0.001	0.002	0.008	0.001	0.001	0.001	0.004	0.015
50	0.001	0.001	0.001	0.001	0.037	0.008	0.001	0.172	0.558	0.988

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: 6-Hydroxyflavone



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 60	100 ± 72	100 ± 89	100 ± 75	100 ± 71	100 ± 138	100 ± 75	100 ± 112	100 ± 103	100 ± 120	16
1	97 ± 87	140 ± 118	89 ± 100	110 ± 115	87 ± 89	107 ± 107	85 ± 95	110 ± 113	73 ± 53	42 ± 40	16
5	316 ± 130	261 ± 154	201 ± 103	117 ± 126	40 ± 41	45 ± 55	45 ± 51	35 ± 30	39 ± 50	30 ± 30	16
10	418 ± 203	485 ± 325	362 ± 323	361 ± 338	254 ± 322	147 ± 191	69 ± 71	66 ± 70	95 ± 168	55 ± 75	16
25	178 ± 70	143 ± 132	313 ± 152	450 ± 231	474 ± 247	338 ± 185	256 ± 172	178 ± 150	149 ± 138	96 ± 106	16
50	351 ± 127	230 ± 155	382 ± 231	454 ± 222	445 ± 211	365 ± 193	288 ± 205	252 ± 174	230 ± 162	201 ± 144	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	70-130	64-136	55-145	62-138	65-135	31-169	63-137	44-156	49-151	40-160
1	53-140	81-199	39-138	53-167	43-132	53-160	38-133	53-166	46-99	22-61
5	251-382	184-337	149-253	54-180	19-60	17-73	19-70	19-50	14-64	15-45
10	316-519	322-648	200-524	192-530	93-414	51-242	34-105	31-101	11-179	18-92
25	143-212	77-209	237-389	334-565	351-598	245-431	170-342	103-253	80-218	42-149
50	288-415	152-307	266-497	343-565	339-550	269-461	185-390	165-339	149-311	129-273

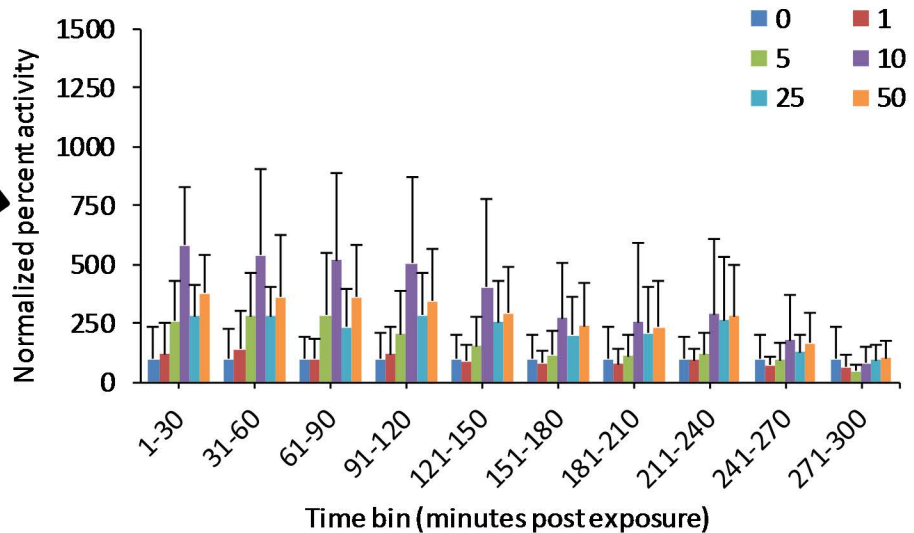
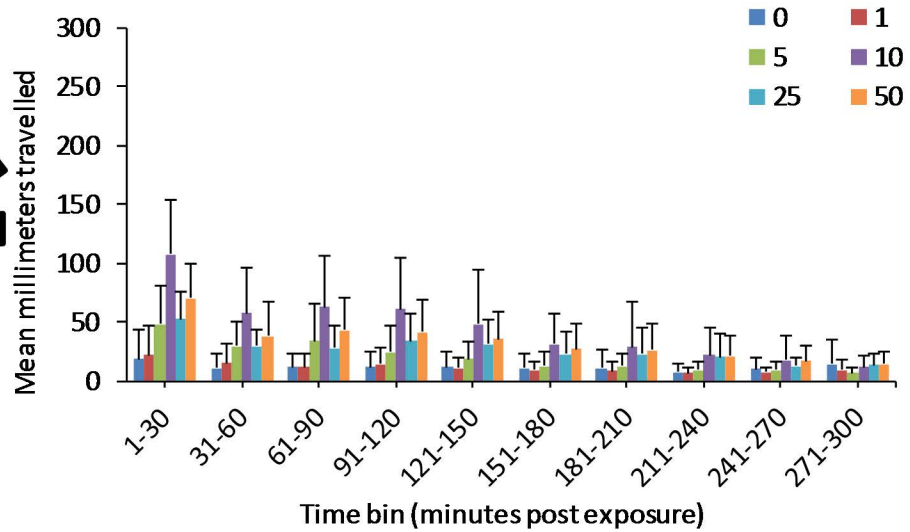
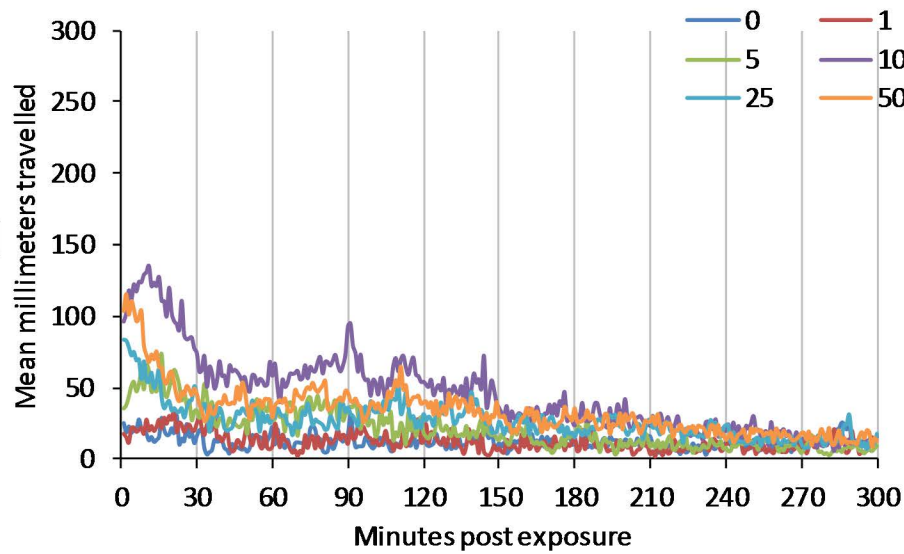
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.926	0.995	0.963	0.981	0.954	1.000	0.908	1.000	0.991	0.206
5	0.001	0.006	0.035	1.000	0.138	0.276	0.096	0.206	0.098	0.038
10	0.001	0.001	0.001	0.003	0.471	1.000	0.549	0.840	0.959	0.457
25	0.164	0.967	0.001	0.001	0.001	0.001	0.034	0.330	0.768	1.000
50	0.001	0.030	0.001	0.001	0.001	0.001	0.009	0.003	0.024	0.056

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: 7-Hydroxyflavone



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 135	100 ± 124	100 ± 96	100 ± 112	100 ± 106	100 ± 106	100 ± 133	100 ± 90	100 ± 104	100 ± 139	16
1	19 ± 133	140 ± 160	96 ± 91	120 ± 120	90 ± 70	83 ± 55	77 ± 66	93 ± 49	73 ± 37	66 ± 54	16
5	261 ± 172	280 ± 188	284 ± 265	205 ± 187	155 ± 124	115 ± 107	111 ± 91	121 ± 89	93 ± 79	46 ± 33	16
10	580 ± 253	539 ± 365	519 ± 367	504 ± 366	402 ± 378	273 ± 234	255 ± 336	287 ± 319	179 ± 195	80 ± 72	16
25	281 ± 129	280 ± 125	233 ± 161	283 ± 186	257 ± 175	200 ± 164	207 ± 199	263 ± 273	129 ± 75	93 ± 69	16
50	377 ± 164	359 ± 268	360 ± 225	343 ± 226	293 ± 194	238 ± 187	232 ± 198	282 ± 218	168 ± 126	101 ± 72	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	33-167	38-162	52-148	44-156	47-153	47-153	33-167	55-145	48-152	30-170
1	52-185	60-220	51-142	60-180	55-125	55-110	44-110	69-118	54-91	39-93
5	175-347	186-374	151-416	112-299	93-217	61-168	65-157	76-166	54-133	30-63
10	453-706	356-722	335-702	321-687	213-591	156-390	87-424	128-447	81-276	45-116
25	217-346	218-343	152-313	190-376	169-345	118-282	107-306	127-399	92-167	59-127
50	295-459	225-493	248-473	230-456	196-390	144-332	133-331	173-390	105-231	64-137

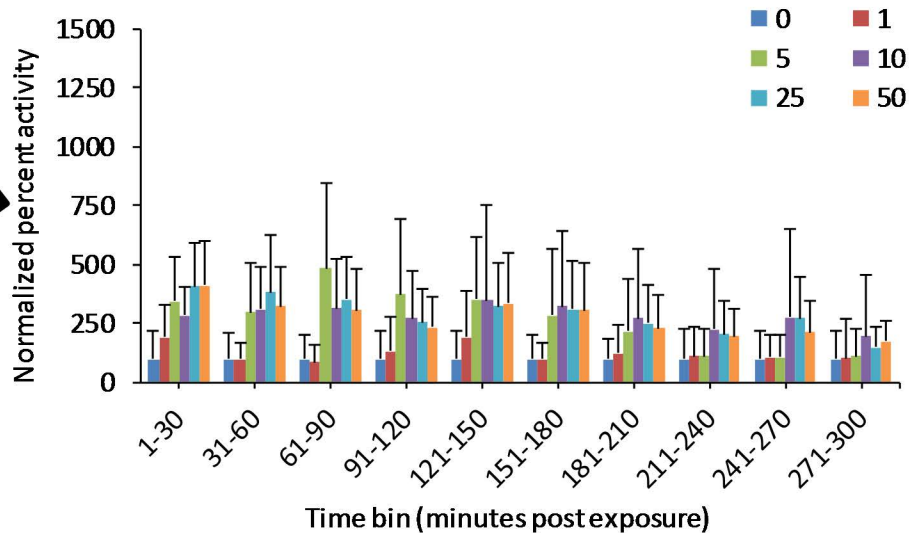
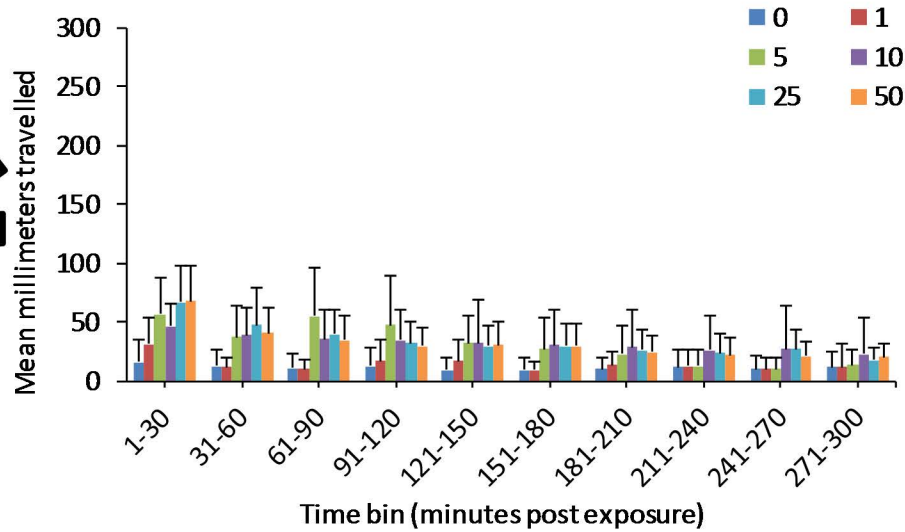
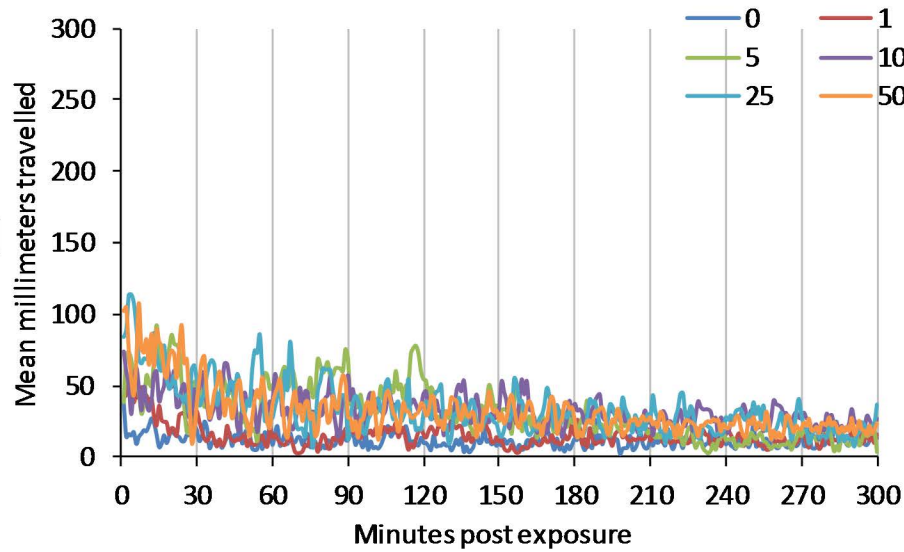
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.999	0.931	0.999	0.982	0.998	1.000	1.000	0.999	1.000	1.000
5	0.001	0.001	0.001	0.044	0.384	1.000	0.996	0.996	0.999	0.816
10	0.001	0.001	0.001	0.001	0.001	0.012	0.038	0.064	0.610	1.000
25	0.001	0.001	0.004	0.001	0.001	0.070	0.032	0.026	0.756	0.888
50	0.001	0.001	0.001	0.001	0.001	0.019	0.025	0.021	0.366	0.853

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

**CHEMICAL:  $\alpha$ -Naphthoflavone**



**Normalized percent activity**

	Time bin (minutes post exposure)										
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 117	100 $\pm$ 115	100 $\pm$ 101	100 $\pm$ 118	100 $\pm$ 120	100 $\pm$ 102	100 $\pm$ 88	100 $\pm$ 129	100 $\pm$ 122	100 $\pm$ 115	16
1	192 $\pm$ 133	97 $\pm$ 68	87 $\pm$ 69	132 $\pm$ 150	190 $\pm$ 202	97 $\pm$ 74	125 $\pm$ 119	112 $\pm$ 125	105 $\pm$ 100	102 $\pm$ 170	16
5	343 $\pm$ 189	296 $\pm$ 212	484 $\pm$ 364	373 $\pm$ 325	353 $\pm$ 261	286 $\pm$ 284	216 $\pm$ 226	110 $\pm$ 116	107 $\pm$ 93	112 $\pm$ 113	16
10	285 $\pm$ 118	311 $\pm$ 181	313 $\pm$ 215	273 $\pm$ 201	349 $\pm$ 408	323 $\pm$ 316	273 $\pm$ 294	225 $\pm$ 254	274 $\pm$ 373	196 $\pm$ 263	16
25	407 $\pm$ 186	381 $\pm$ 247	352 $\pm$ 179	256 $\pm$ 143	321 $\pm$ 186	309 $\pm$ 204	249 $\pm$ 169	205 $\pm$ 143	271 $\pm$ 176	148 $\pm$ 88	16
50	413 $\pm$ 186	322 $\pm$ 172	305 $\pm$ 176	234 $\pm$ 128	335 $\pm$ 213	308 $\pm$ 199	230 $\pm$ 138	194 $\pm$ 122	213 $\pm$ 132	175 $\pm$ 91	16

**Mean  $\pm$  standard deviation**

**Normalized percent activity**

	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	42-158	43-157	50-150	41-159	40-160	49-151	56-144	35-165	39-161	42-158
1	125-259	63-131	53-122	57-207	89-291	60-134	66-184	49-174	55-155	17-187
5	249-438	190-402	302-666	210-535	222-483	144-427	103-329	52-169	60-153	55-168
10	227-344	221-401	205-420	172-373	145-553	165-481	126-421	98-353	88-461	65-328
25	314-501	258-505	262-441	185-328	228-414	207-411	165-334	134-277	183-359	104-192
50	320-505	236-408	217-393	170-297	229-442	208-407	161-299	133-255	147-279	130-220

**95% confidence interval**

**p-values**

	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.046	0.999	1.000	0.926	0.445	1.000	0.998	0.962	0.998	1.000
5	0.001	0.002	0.001	0.001	0.001	0.012	0.437	0.994	1.000	1.000
10	0.001	0.001	0.001	0.001	0.003	0.001	0.020	0.024	0.053	0.356
25	0.001	0.001	0.001	0.001	0.001	0.002	0.045	0.054	0.015	0.485
50	0.001	0.001	0.001	0.002	0.001	0.001	0.032	0.025	0.052	0.106

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: $\beta$ -Naphthoflavone

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 $\pm$ 93	100 $\pm$ 105	100 $\pm$ 92	100 $\pm$ 89	100 $\pm$ 86	100 $\pm$ 85	100 $\pm$ 120	100 $\pm$ 88	100 $\pm$ 78	100 $\pm$ 64	16
1	119 $\pm$ 109	116 $\pm$ 98	93 $\pm$ 111	83 $\pm$ 95	116 $\pm$ 124	84 $\pm$ 85	67 $\pm$ 67	130 $\pm$ 145	112 $\pm$ 130	166 $\pm$ 264	16
5	138 $\pm$ 147	136 $\pm$ 110	115 $\pm$ 77	94 $\pm$ 80	84 $\pm$ 40	136 $\pm$ 160	119 $\pm$ 139	157 $\pm$ 139	110 $\pm$ 82	162 $\pm$ 137	16
10	118 $\pm$ 103	179 $\pm$ 164	150 $\pm$ 109	85 $\pm$ 67	114 $\pm$ 100	102 $\pm$ 98	74 $\pm$ 50	126 $\pm$ 63	116 $\pm$ 80	103 $\pm$ 75	16
25	110 $\pm$ 107	155 $\pm$ 139	110 $\pm$ 89	87 $\pm$ 132	107 $\pm$ 142	124 $\pm$ 174	83 $\pm$ 102	144 $\pm$ 133	122 $\pm$ 157	137 $\pm$ 179	16
50	267 $\pm$ 259	190 $\pm$ 126	324 $\pm$ 245	106 $\pm$ 110	102 $\pm$ 79	97 $\pm$ 84	90 $\pm$ 78	121 $\pm$ 80	129 $\pm$ 103	129 $\pm$ 105	16

## Mean $\pm$ standard deviation

## Normalized percent activity

## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	53-147	47-153	54-146	56-144	57-143	58-142	40-160	56-144	61-139	68-132
1	65-174	67-165	38-149	35-130	54-178	41-126	34-101	58-202	47-177	34-298
5	64-211	81-191	77-154	54-134	64-104	56-215	50-189	88-227	69-151	94-231
10	67-170	97-260	95-205	52-119	64-165	53-151	49-99	95-158	76-156	65-140
25	57-164	60-249	15-204	21-153	35-178	37-211	32-134	53-236	43-200	47-226
50	137-397	127-254	201-447	51-162	62-141	55-139	51-129	81-162	78-181	76-181

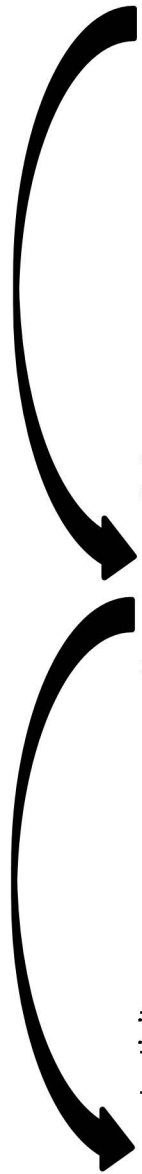
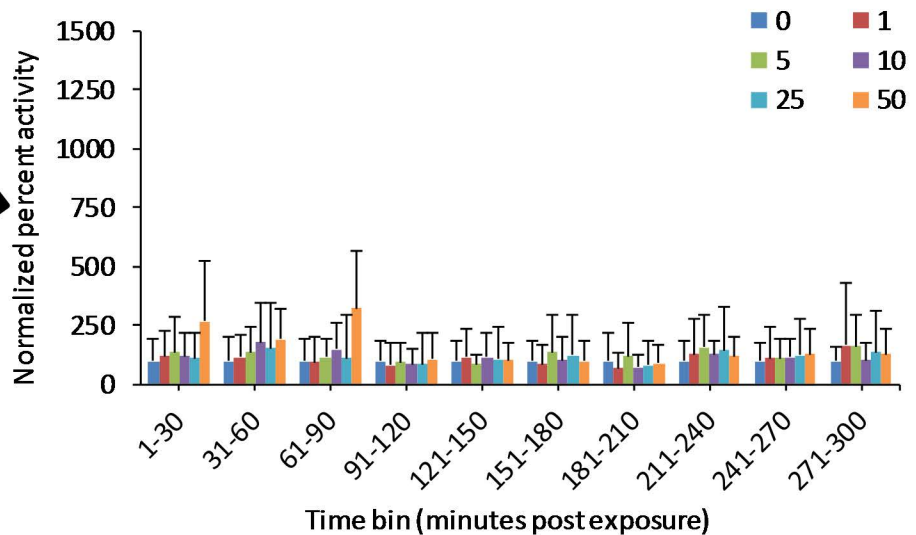
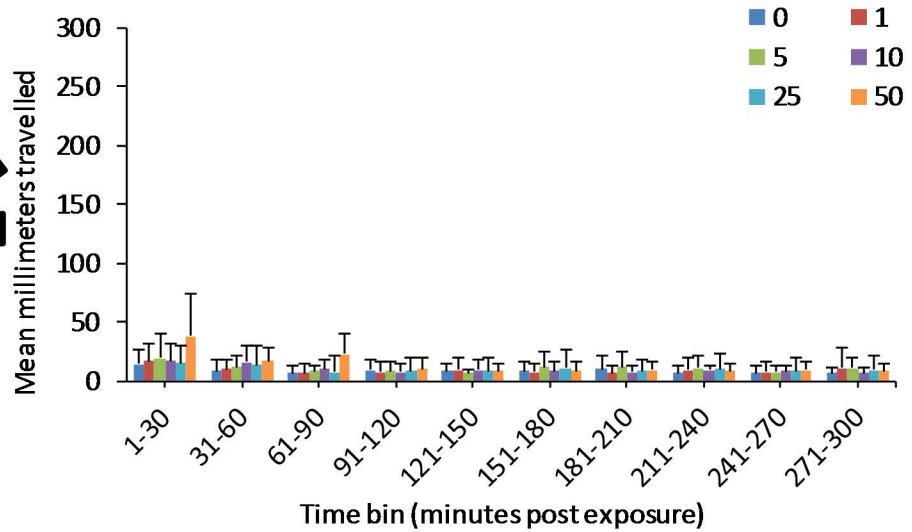
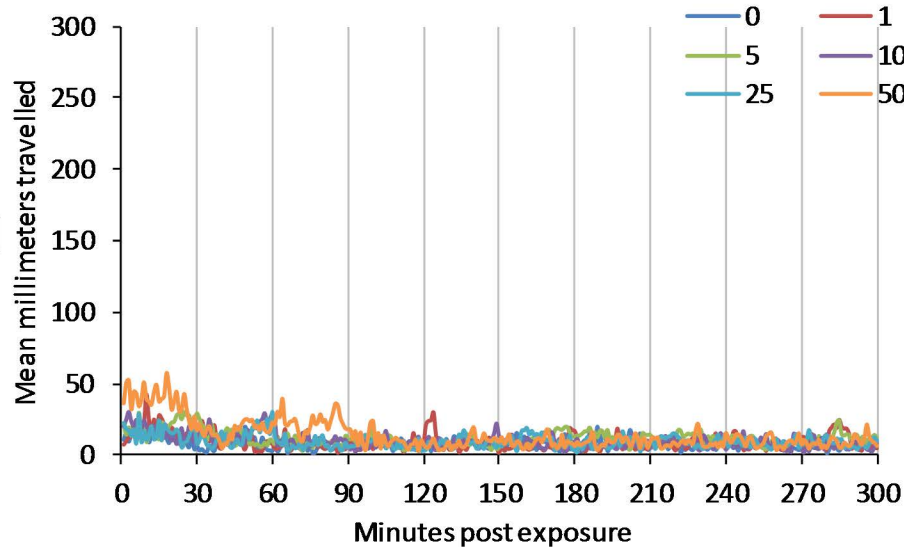
## 95% confidence interval

## p-values

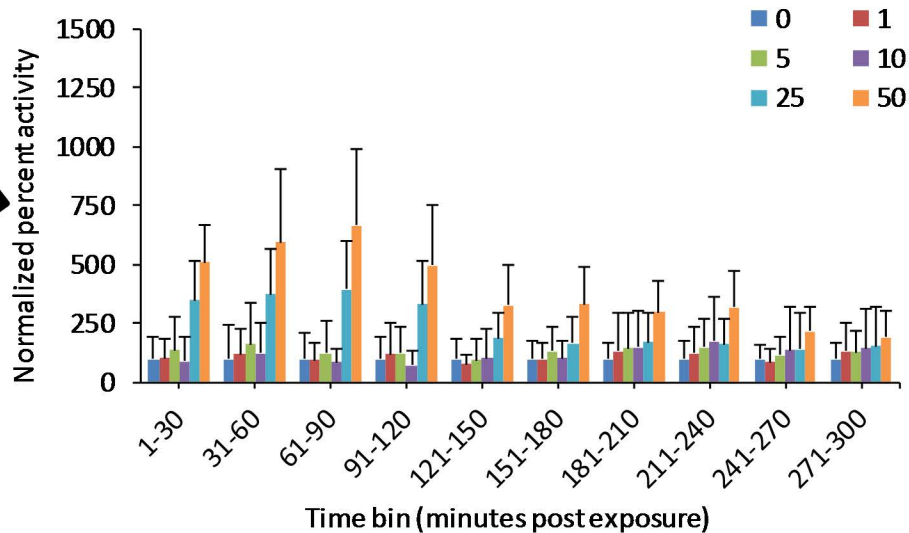
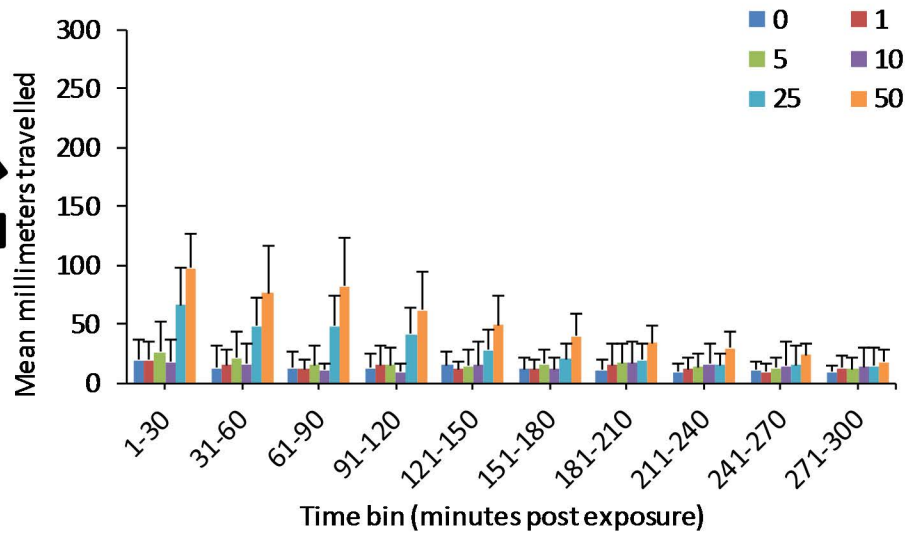
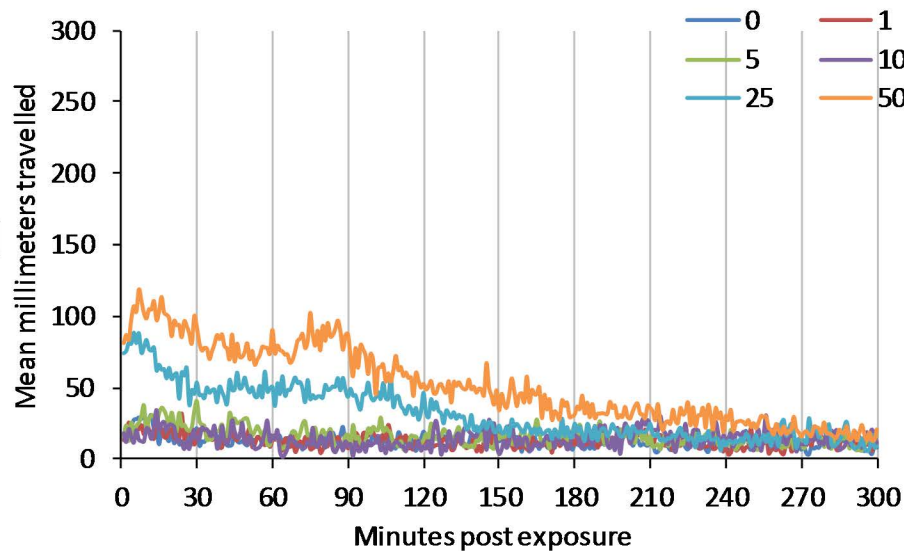
## Time bin (minutes post exposure)

[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.969	0.982	1.000	0.966	1.000	0.985	0.964	0.983	1.000	1.000
5	0.771	0.871	0.977	1.000	1.000	0.979	0.954	0.527	0.960	0.838
10	0.944	0.261	0.645	1.000	0.994	1.000	1.000	0.740	0.960	1.000
25	0.938	0.962	1.000	0.930	1.000	1.000	1.000	0.958	0.993	1.000
50	0.010	0.153	0.003	1.000	1.000	1.000	1.000	0.948	0.931	0.994

## Two-way repeated measures ANOVA, Tukey's post-hoc, $p \leq 0.05$



# CHEMICAL: Apigenin



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 92	100 ± 142	100 ± 111	100 ± 97	100 ± 82	100 ± 78	100 ± 72	100 ± 74	100 ± 64	100 ± 65	16
1	102 ± 84	119 ± 106	95 ± 73	119 ± 134	77 ± 45	97 ± 69	133 ± 161	125 ± 115	87 ± 60	134 ± 115	16
5	138 ± 137	162 ± 176	125 ± 136	123 ± 113	95 ± 90	131 ± 108	146 ± 150	147 ± 123	116 ± 77	129 ± 92	16
10	91 ± 99	123 ± 131	88 ± 53	74 ± 61	103 ± 126	101 ± 76	150 ± 157	174 ± 193	136 ± 187	144 ± 168	16
25	347 ± 165	374 ± 188	394 ± 208	331 ± 185	186 ± 112	168 ± 108	172 ± 127	161 ± 110	140 ± 153	155 ± 169	16
50	509 ± 165	593 ± 309	668 ± 324	496 ± 259	325 ± 173	331 ± 162	296 ± 132	318 ± 157	217 ± 100	190 ± 115	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	54-146	29-171	45-155	51-149	59-141	61-139	64-136	63-137	68-132	68-132
1	59-144	66-172	58-131	52-186	54-99	62-131	52-214	67-182	57-117	76-191
5	69-207	74-250	58-193	66-179	50-140	77-185	71-221	86-209	78-155	83-175
10	42-141	58-189	61-114	44-105	40-166	64-139	71-228	78-271	43-230	60-229
25	265-430	280-468	290-498	239-424	129-242	114-221	108-235	106-216	63-216	71-240
50	432-586	438-747	506-830	366-625	239-411	250-412	229-362	240-396	167-267	132-247

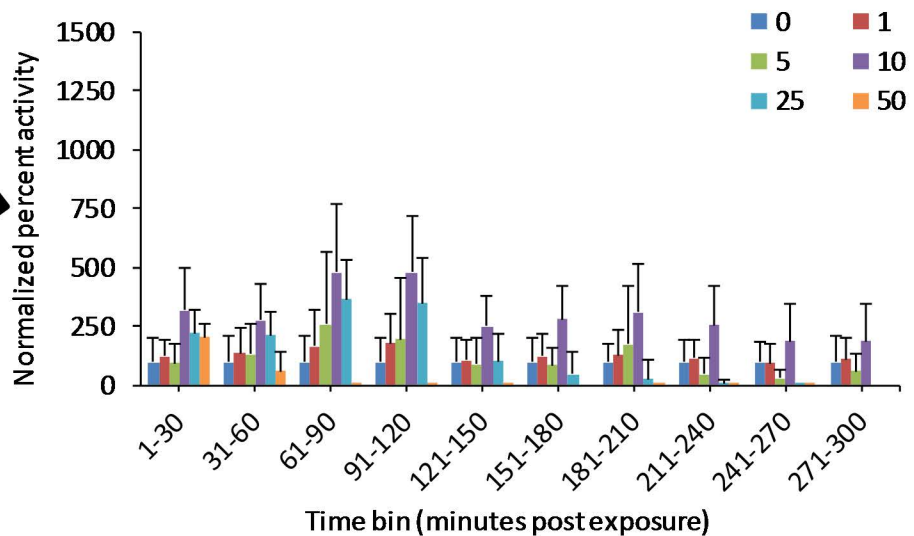
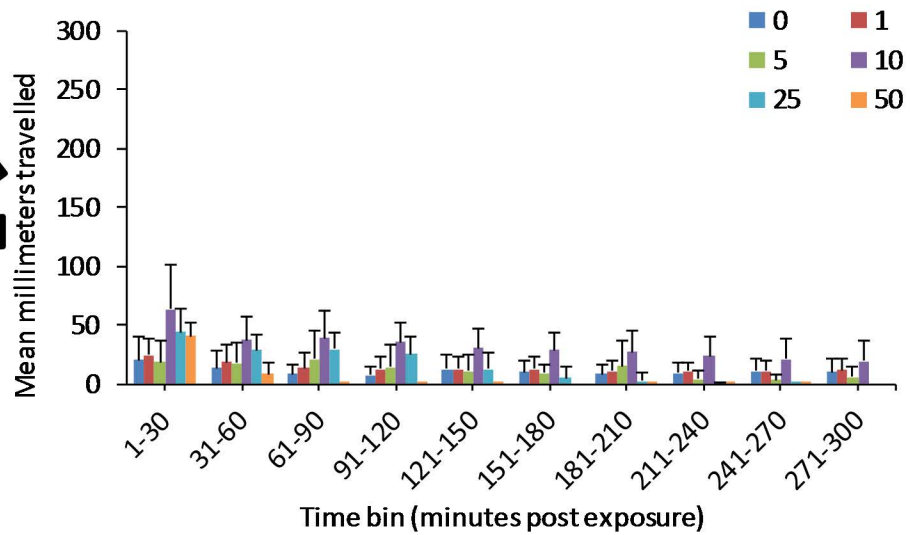
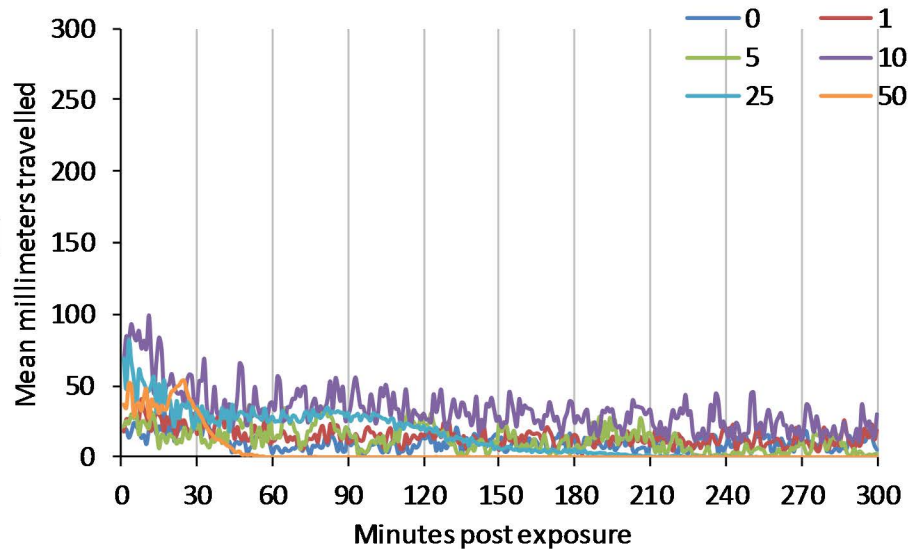
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	1.000	0.740	1.000	0.998	0.996	1.000	0.995	0.987	0.998	0.944
5	0.954	0.349	0.994	0.977	0.999	0.987	0.988	0.780	0.995	0.881
10	1.000	0.679	1.000	0.869	1.000	1.000	0.939	0.698	1.000	0.917
25	0.001	0.001	0.001	0.001	0.094	0.266	0.324	0.457	0.993	0.773
50	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.018	0.105

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Biochanin A



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 103	100 ± 110	100 ± 114	100 ± 100	100 ± 100	100 ± 98	100 ± 79	100 ± 97	100 ± 87	100 ± 109	16
1	122 ± 72	137 ± 109	168 ± 156	178 ± 129	105 ± 90	124 ± 98	128 ± 104	116 ± 81	95 ± 82	111 ± 94	16
5	94 ± 87	132 ± 130	258 ± 312	197 ± 258	89 ± 117	87 ± 77	176 ± 250	47 ± 72	31 ± 35	60 ± 78	16
10	317 ± 184	278 ± 150	480 ± 286	481 ± 237	250 ± 130	281 ± 144	309 ± 204	253 ± 171	186 ± 161	187 ± 159	16
25	220 ± 99	212 ± 99	364 ± 170	346 ± 191	102 ± 118	47 ± 94	25 ± 86	4 ± 18	1 ± 2	0 ± 0	16
50	202 ± 57	60 ± 79	0 ± 1	0 ± 0	0 ± 1	0 ± 0	0 ± 0	0 ± 1	0 ± 0	0 ± 0	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	48-152	45-155	43-157	50-150	50-150	51-149	60-140	52-148	57-143	45-155
1	86-158	82-191	89-246	114-242	60-150	75-173	75-180	76-157	54-136	64-158
5	51-137	67-198	102-414	68-326	31-148	48-125	51-301	11-83	13-48	21-98
10	225-409	202-353	337-623	362-599	185-315	209-353	207-410	168-339	106-267	108-266
25	171-270	163-261	279-449	250-442	43-161	0-94	-18-68	-4-13	0-2	0-0
50	174-231	20-99	0-1	0-0	0-1	0-0	0-0	0-0	0-0	0-0

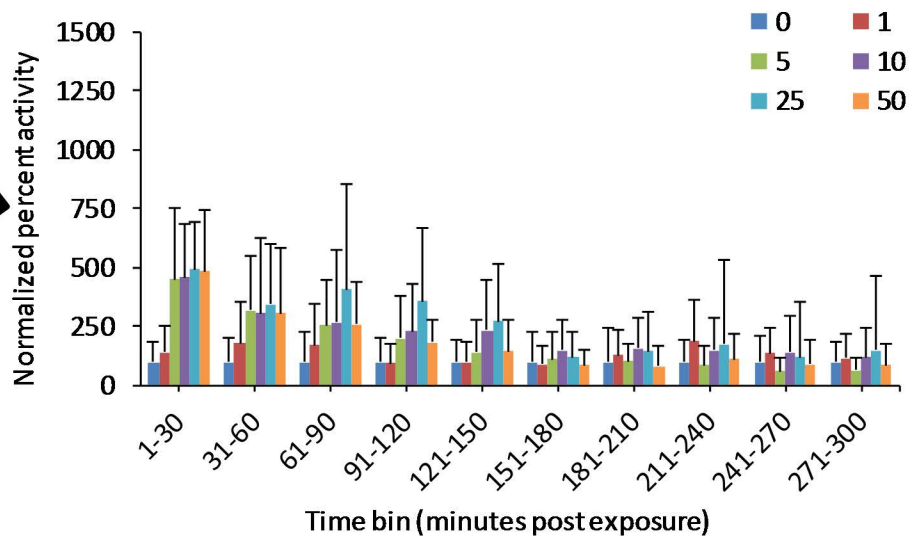
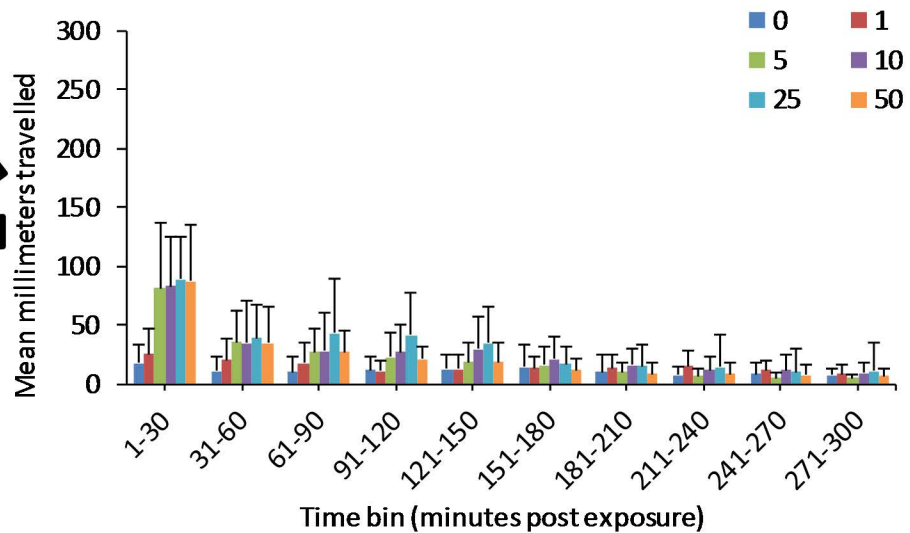
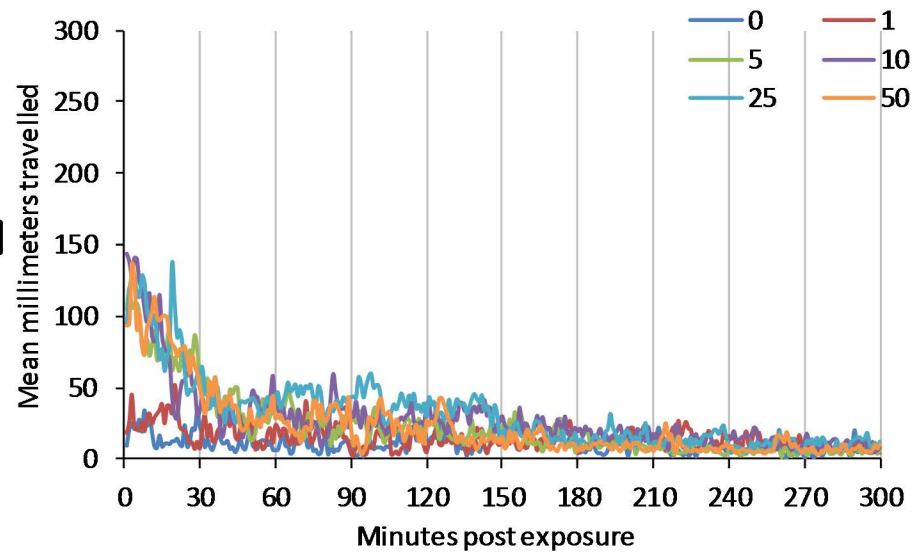
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.711	0.403	0.594	0.347	1.000	0.783	0.986	0.930	0.999	0.992
5	1.000	0.837	0.464	0.988	0.843	0.999	1.000	0.037	0.003	0.315
10	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.004	0.411	0.134
25	0.001	0.001	0.001	0.001	0.800	0.001	0.001	0.001	0.001	0.001
50	0.001	0.146	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Chrysin



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 83	100 ± 103	100 ± 129	100 ± 100	100 ± 98	100 ± 129	100 ± 146	100 ± 94	100 ± 114	100 ± 84	16
1	140 ± 116	180 ± 171	172 ± 171	93 ± 82	96 ± 93	92 ± 73	128 ± 105	186 ± 175	137 ± 108	116 ± 102	16
5	448 ± 305	317 ± 231	255 ± 194	199 ± 179	142 ± 134	111 ± 113	101 ± 75	86 ± 86	62 ± 53	66 ± 51	16
10	457 ± 231	308 ± 316	269 ± 302	229 ± 203	232 ± 218	149 ± 126	157 ± 131	149 ± 138	139 ± 155	120 ± 127	16
25	492 ± 200	345 ± 254	409 ± 443	357 ± 311	271 ± 243	119 ± 106	144 ± 171	176 ± 356	118 ± 239	150 ± 318	16
50	483 ± 262	307 ± 278	261 ± 174	181 ± 97	146 ± 130	84 ± 69	81 ± 89	110 ± 108	90 ± 103	87 ± 91	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	58-142	48-152	36-164	50-150	51-149	36-164	27-173	53-147	43-157	58-142
1	83-198	94-265	86-257	52-134	50-143	55-128	76-181	99-274	83-191	65-168
5	295-600	201-432	158-352	110-289	75-209	55-168	64-139	43-129	35-88	41-92
10	342-572	149-466	118-420	127-330	123-341	86-212	92-223	80-218	61-217	57-184
25	392-592	218-472	187-631	202-513	150-392	66-171	59-230	-2-353	-1-238	-9-309
50	352-614	168-446	174-349	133-229	81-211	50-119	37-126	56-164	38-142	41-132

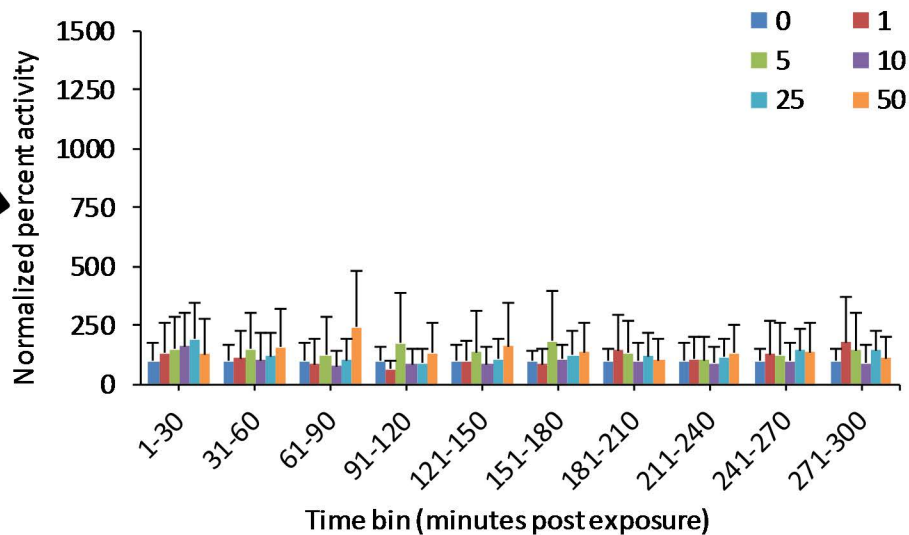
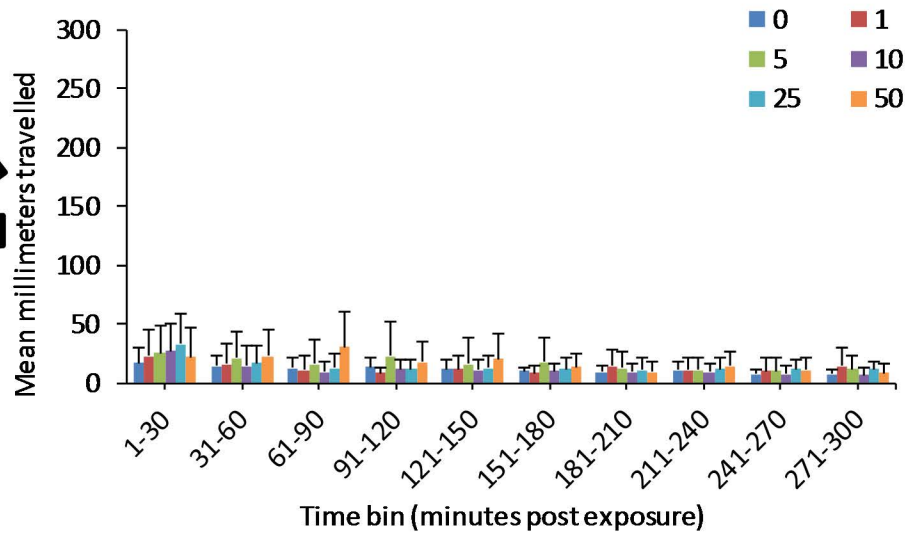
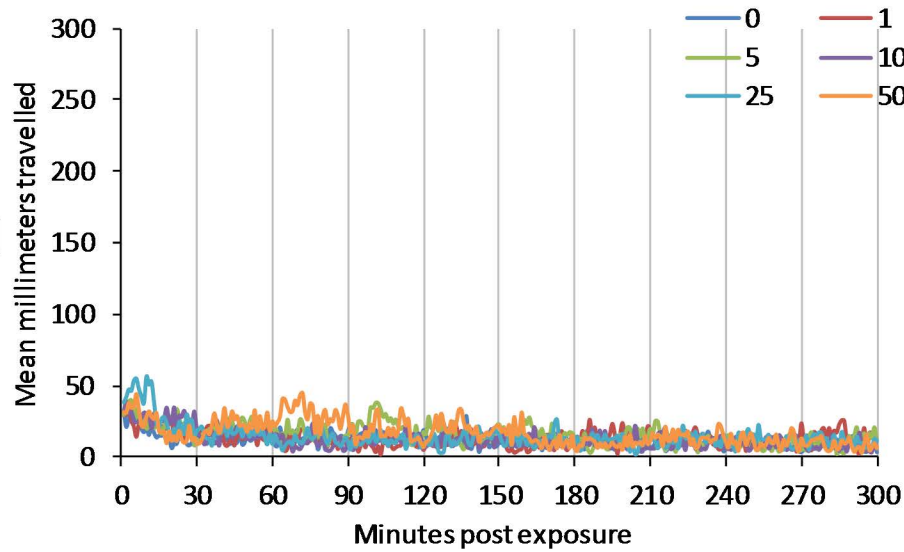
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.886	0.469	0.366	1.000	1.000	1.000	0.539	0.501	0.836	1.000
5	0.001	0.001	0.002	0.293	0.846	0.998	0.965	0.974	0.795	0.893
10	0.001	0.001	0.003	0.072	0.135	0.661	0.280	0.936	0.993	1.000
25	0.001	0.001	0.001	0.001	0.025	0.984	0.712	1.000	0.934	1.000
50	0.001	0.001	0.002	0.101	0.868	0.995	0.996	0.998	0.894	0.873

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Daidzein



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 77	100 ± 64	100 ± 76	100 ± 64	100 ± 69	100 ± 40	100 ± 51	100 ± 78	100 ± 48	100 ± 50	16
1	132 ± 132	111 ± 120	86 ± 103	66 ± 38	97 ± 90	87 ± 65	146 ± 145	106 ± 97	129 ± 139	177 ± 198	16
5	151 ± 137	151 ± 152	126 ± 164	173 ± 217	135 ± 175	181 ± 220	131 ± 143	103 ± 99	123 ± 136	146 ± 156	16
10	160 ± 140	104 ± 115	76 ± 67	87 ± 62	87 ± 71	105 ± 61	97 ± 80	91 ± 71	100 ± 77	90 ± 74	16
25	193 ± 155	120 ± 102	102 ± 90	89 ± 63	107 ± 90	126 ± 102	119 ± 101	115 ± 81	145 ± 95	145 ± 86	16
50	129 ± 151	158 ± 161	241 ± 241	134 ± 127	164 ± 179	135 ± 128	101 ± 95	132 ± 118	135 ± 131	111 ± 89	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	62-138	68-132	62-138	68-132	65-135	80-120	74-126	61-139	76-124	75-125
1	66-198	51-171	35-138	47-85	52-142	54-120	74-219	57-154	59-199	78-276
5	82-219	75-227	44-208	64-282	47-222	71-291	59-202	54-153	54-191	67-224
10	90-230	47-162	42-109	56-118	52-123	75-136	57-138	55-127	61-138	53-127
25	115-271	69-171	57-147	57-120	62-152	75-176	68-170	74-155	98-193	102-188
50	54-204	78-239	121-362	70-198	74-253	71-199	53-149	73-191	69-200	67-156

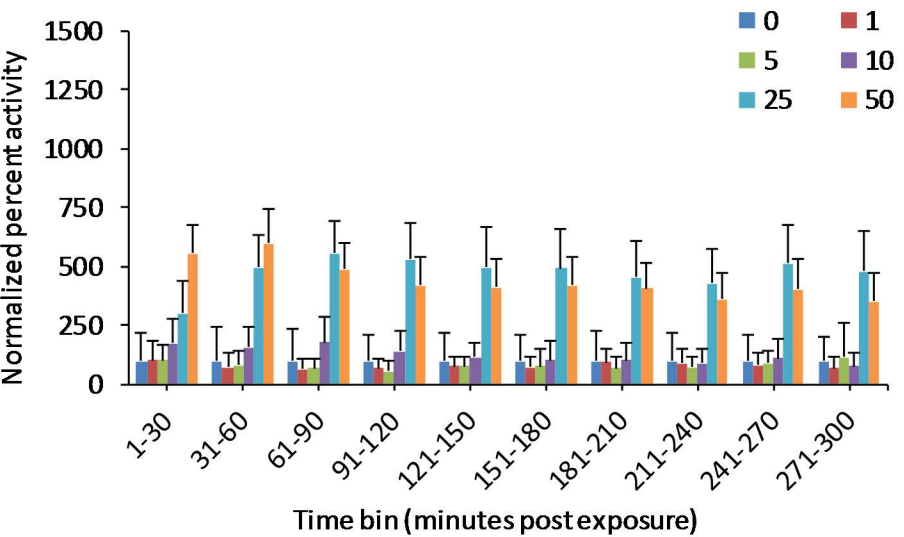
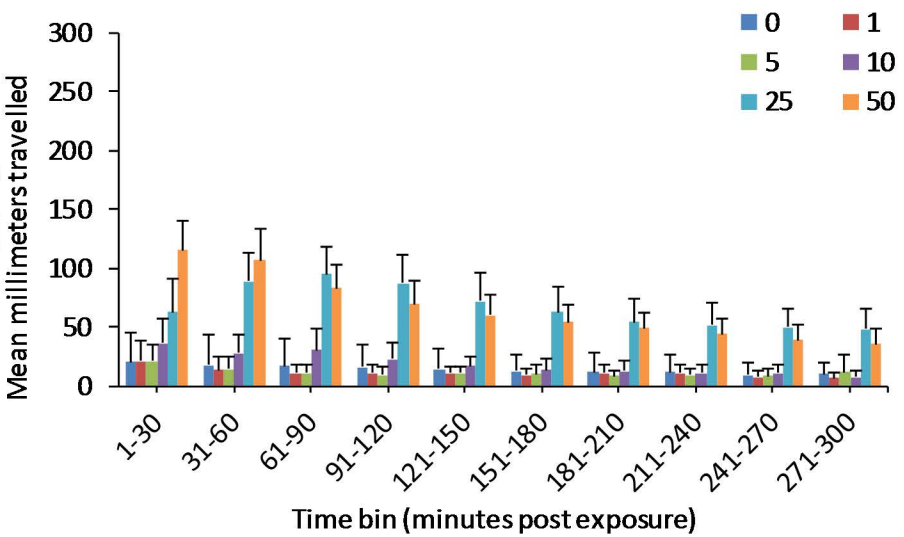
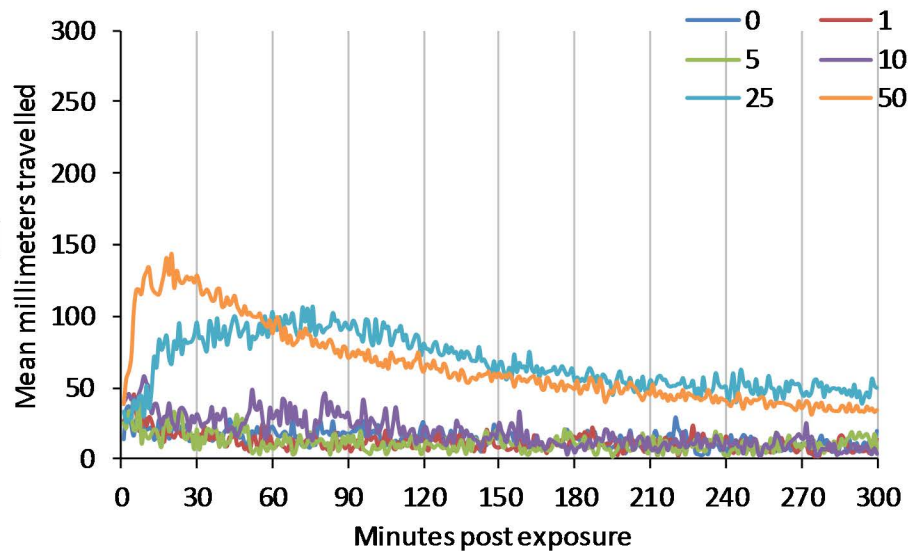
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.974	0.979	0.989	0.827	0.976	0.844	1.000	0.999	1.000	0.987
5	0.855	0.993	0.998	0.999	1.000	0.996	1.000	1.000	1.000	0.990
10	0.974	0.985	0.768	0.993	0.978	1.000	0.984	0.990	0.997	0.974
25	0.463	1.000	1.000	0.999	1.000	1.000	1.000	1.000	0.981	0.904
50	1.000	0.993	0.447	0.999	0.971	1.000	0.996	0.995	1.000	1.000

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: (S)-Equisol



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 121	100 ± 144	100 ± 140	100 ± 109	100 ± 121	100 ± 109	100 ± 131	100 ± 121	100 ± 113	100 ± 105	16
1	103 ± 80	75 ± 61	63 ± 43	68 ± 42	76 ± 40	74 ± 44	95 ± 58	91 ± 57	81 ± 56	70 ± 43	16
5	103 ± 66	80 ± 61	67 ± 42	56 ± 46	76 ± 41	77 ± 71	70 ± 45	74 ± 47	88 ± 58	117 ± 147	16
10	175 ± 104	156 ± 92	130 ± 105	140 ± 87	117 ± 56	103 ± 84	104 ± 70	89 ± 66	112 ± 79	78 ± 61	16
25	304 ± 132	498 ± 136	554 ± 137	529 ± 151	495 ± 169	490 ± 168	454 ± 159	429 ± 150	515 ± 163	478 ± 170	16
50	558 ± 121	597 ± 150	486 ± 113	422 ± 123	411 ± 118	421 ± 116	406 ± 109	361 ± 115	404 ± 131	352 ± 125	16

Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	40-160	28-172	30-170	46-154	40-160	45-155	34-166	39-161	43-157	47-153
1	63-143	44-106	42-84	47-89	56-96	52-96	66-124	62-119	53-109	48-92
5	70-136	50-111	46-88	33-79	55-96	42-113	48-93	51-98	59-117	43-111
10	123-227	110-201	127-232	97-184	89-145	62-145	70-139	56-122	73-151	47-108
25	237-370	430-566	486-623	454-605	411-580	406-574	375-533	354-504	434-597	393-563
50	497-618	522-672	430-543	361-483	352-470	363-479	351-460	304-418	339-470	290-414

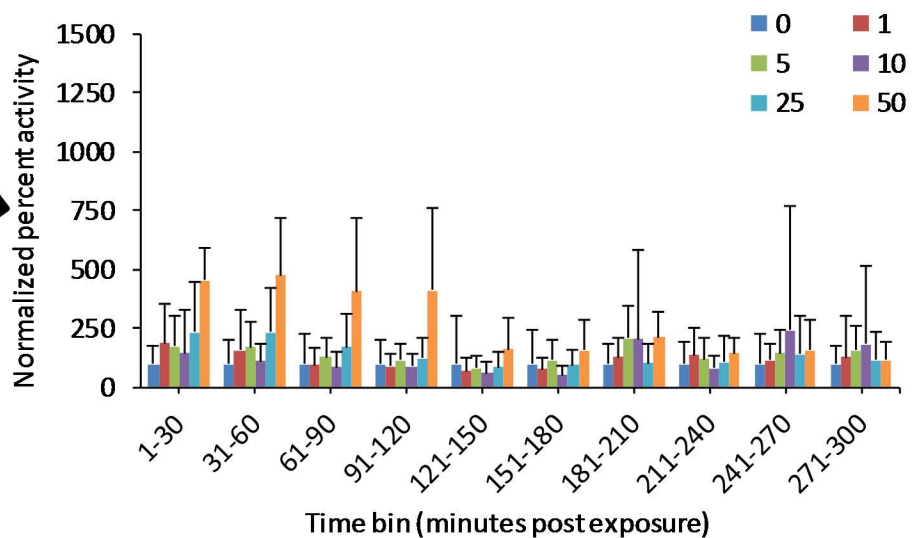
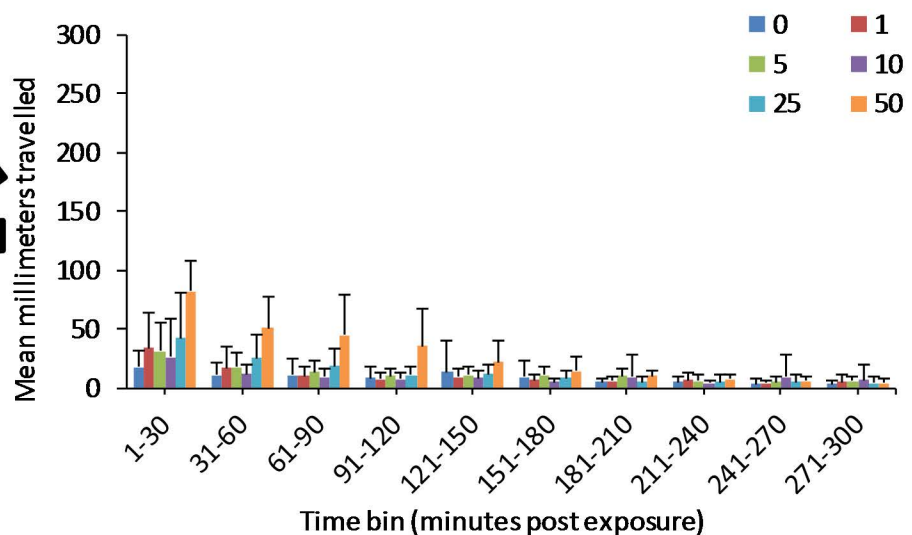
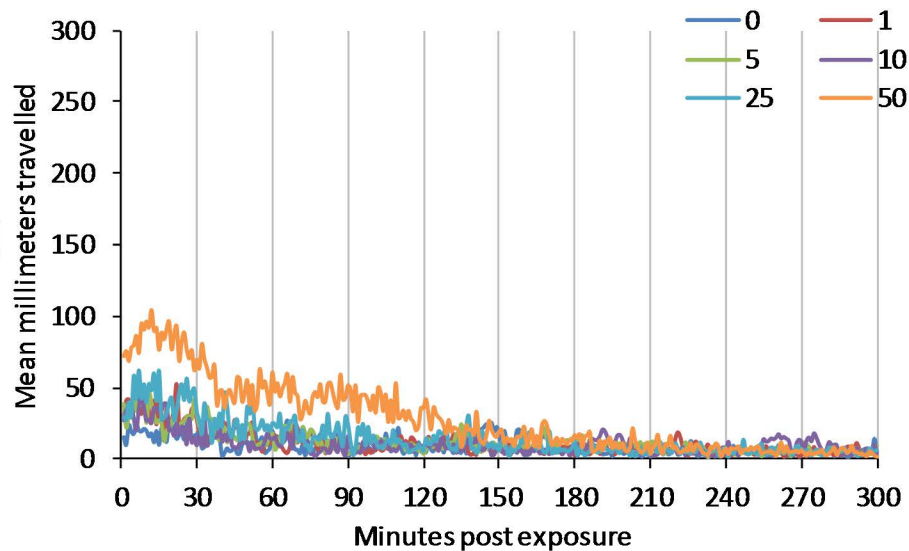
95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.844	1.000	0.999	0.995	1.000	1.000	0.996	1.000	0.997	0.980
5	0.780	0.980	1.000	0.498	1.000	1.000	0.994	0.993	1.000	1.000
10	0.001	0.002	0.001	0.103	0.535	0.962	0.900	1.000	0.975	0.996
25	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
50	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Fisetin



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 78	100 ± 100	100 ± 124	100 ± 102	100 ± 200	100 ± 145	100 ± 81	100 ± 93	100 ± 128	100 ± 78	16
1	187 ± 164	160 ± 172	94 ± 71	90 ± 52	70 ± 55	75 ± 54	130 ± 79	135 ± 116	117 ± 68	126 ± 178	16
5	174 ± 132	170 ± 111	128 ± 85	113 ± 71	83 ± 50	116 ± 83	210 ± 132	121 ± 89	146 ± 98	159 ± 105	16
10	147 ± 181	113 ± 75	87 ± 66	89 ± 57	60 ± 48	53 ± 35	202 ± 382	80 ± 56	244 ± 525	181 ± 337	16
25	235 ± 209	235 ± 188	169 ± 142	124 ± 89	87 ± 62	93 ± 66	101 ± 88	107 ± 115	142 ± 161	115 ± 123	16
50	454 ± 141	473 ± 242	408 ± 312	411 ± 349	160 ± 135	158 ± 131	212 ± 112	144 ± 69	158 ± 126	114 ± 79	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	61-139	50-150	38-162	49-151	0-200	27-173	59-141	53-147	36-164	61-139
1	105-268	73-246	59-130	64-116	43-98	48-102	90-169	77-193	83-151	38-215
5	108-240	114-225	85-170	78-149	58-108	75-158	144-276	76-166	97-195	107-212
10	56-238	75-151	54-120	60-117	36-84	36-71	11-393	52-108	18-506	13-349
25	131-340	141-329	98-240	80-169	56-118	60-126	57-145	50-165	61-222	54-177
50	383-525	353-594	252-564	236-585	92-227	92-224	166-267	110-179	95-221	74-163

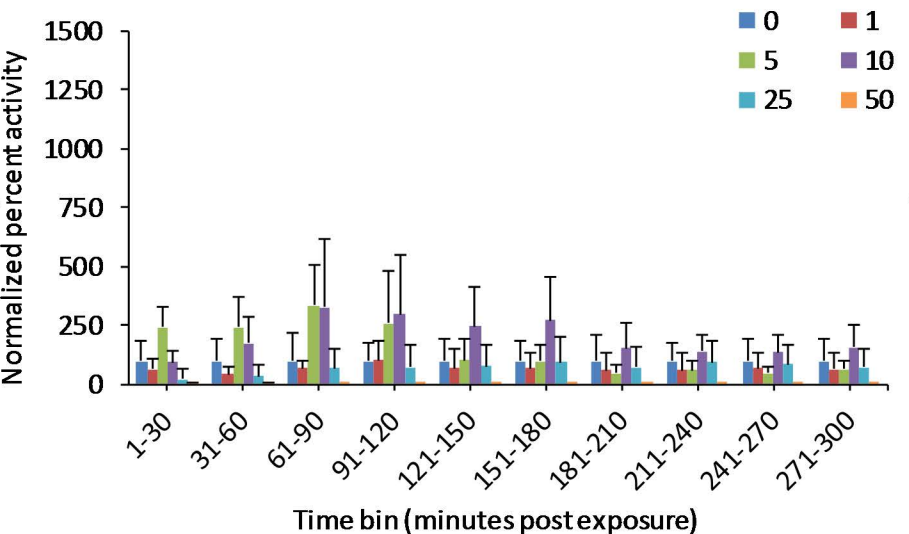
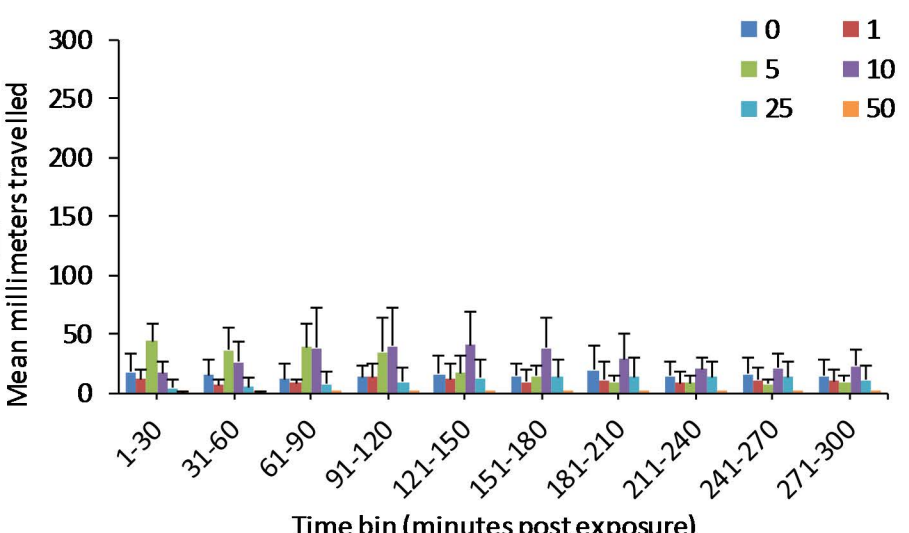
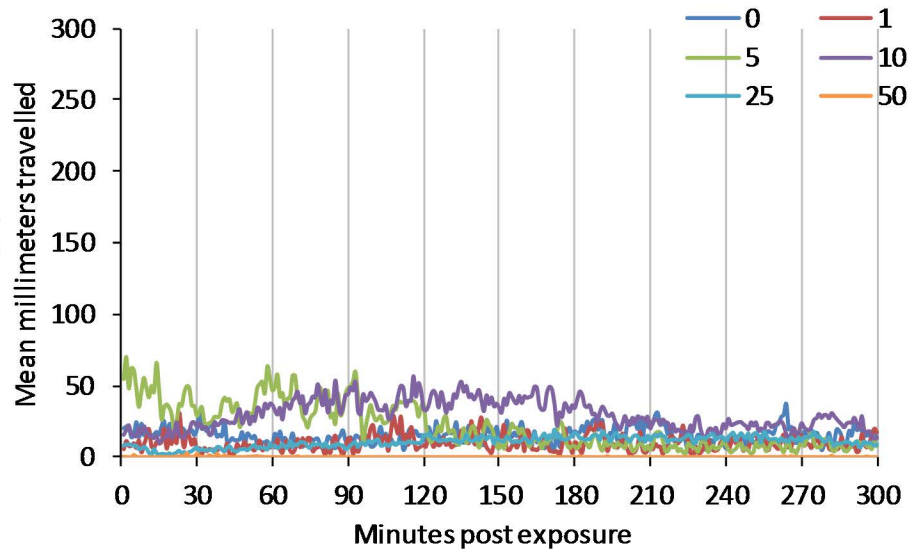
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.461	0.554	0.993	0.994	0.963	0.998	0.834	0.879	0.731	0.998
5	0.413	0.115	0.334	0.853	0.532	0.554	0.073	0.948	0.437	0.428
10	0.997	0.812	0.984	0.999	0.993	0.993	0.671	1.000	0.461	0.918
25	0.155	0.118	0.262	0.946	0.723	0.944	1.000	1.000	0.916	1.000
50	0.001	0.001	0.001	0.001	0.003	0.039	0.029	0.293	0.455	0.995

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Flavone



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 83	100 ± 90	100 ± 118	100 ± 77	100 ± 97	100 ± 81	100 ± 107	100 ± 79	100 ± 92	100 ± 95	16
1	65 ± 42	43 ± 33	69 ± 35	104 ± 82	71 ± 77	67 ± 68	59 ± 80	61 ± 70	68 ± 67	66 ± 70	16
5	242 ± 87	241 ± 130	338 ± 172	261 ± 224	103 ± 89	99 ± 70	48 ± 33	58 ± 43	46 ± 30	63 ± 39	16
10	93 ± 52	176 ± 112	328 ± 289	298 ± 247	245 ± 171	271 ± 189	151 ± 114	140 ± 71	135 ± 80	156 ± 97	16
25	23 ± 44	36 ± 49	68 ± 84	73 ± 95	77 ± 92	94 ± 105	72 ± 87	92 ± 93	86 ± 85	74 ± 80	16
50	1 ± 4	1 ± 6	0 ± 1	0 ± 0	0 ± 0	0 ± 0	0 ± 1	0 ± 0	0 ± 1	0 ± 1	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	58-142	55-145	41-159	62-138	52-148	59-141	46-154	60-140	54-146	53-147
1	43-86	27-60	52-87	63-145	32-109	34-101	19-99	26-96	34-101	31-101
5	199-286	176-306	252-424	149-373	59-148	65-134	31-65	37-80	31-61	44-83
10	67-119	120-232	183-472	175-422	160-330	176-365	94-208	105-176	95-175	107-204
25	1-45	12-61	26-110	25-120	30-123	41-146	28-116	46-139	43-128	33-114
50	-1-3	-1-4	0-1	0-0	0-0	0-0	0-0	0-0	0-1	0-1

## 95% confidence interval

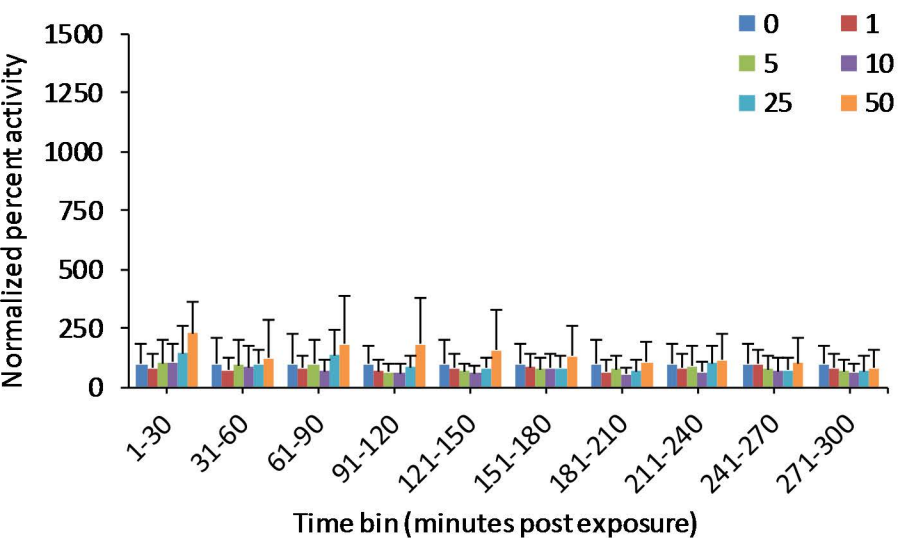
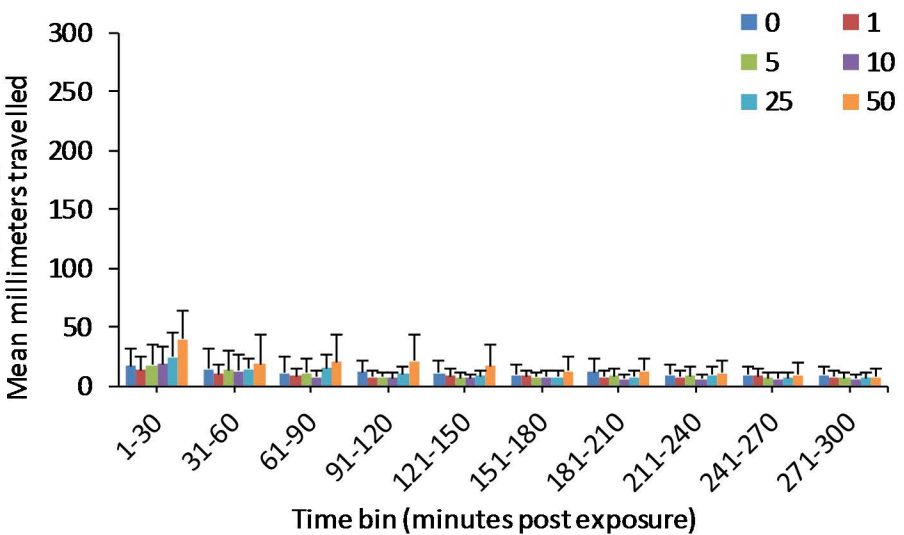
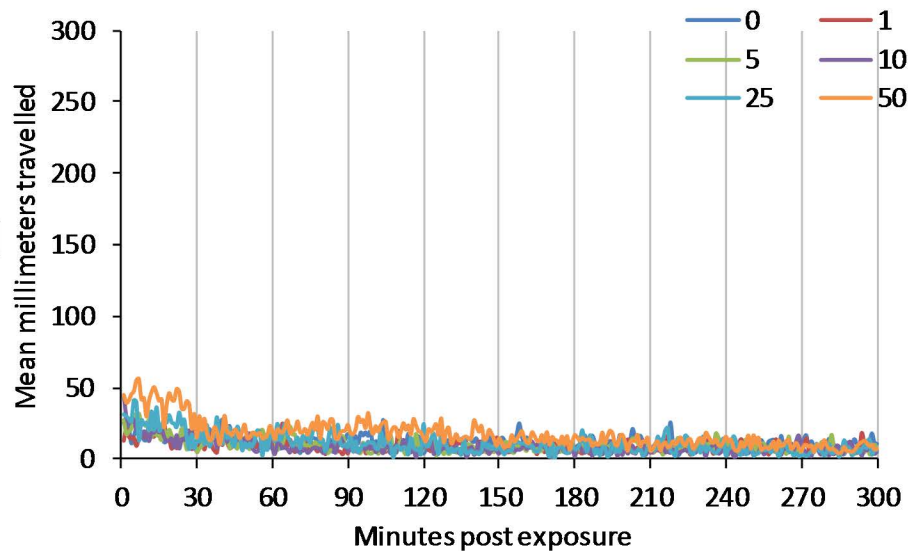
## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.891	0.307	0.998	1.000	0.670	0.538	0.159	0.164	0.558	0.502
5	0.001	0.001	0.001	0.039	1.000	1.000	0.224	0.285	0.123	0.563
10	0.996	0.035	0.001	0.001	0.001	0.002	0.319	0.716	0.741	0.474
25	0.001	0.008	0.475	0.236	0.626	0.930	0.529	0.923	0.859	0.566
50	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Formononetin



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 81	100 ± 111	100 ± 125	100 ± 81	100 ± 104	100 ± 88	100 ± 105	100 ± 86	100 ± 84	100 ± 73	16
1	80 ± 63	71 ± 52	80 ± 55	69 ± 45	81 ± 63	88 ± 52	63 ± 51	84 ± 63	97 ± 64	83 ± 60	16
5	103 ± 98	93 ± 109	100 ± 105	65 ± 38	68 ± 37	78 ± 49	76 ± 58	89 ± 91	79 ± 56	71 ± 50	16
10	108 ± 81	85 ± 91	68 ± 49	61 ± 41	60 ± 35	83 ± 56	55 ± 26	65 ± 47	69 ± 56	65 ± 32	16
25	144 ± 118	99 ± 58	136 ± 112	86 ± 48	82 ± 44	83 ± 49	69 ± 45	101 ± 77	72 ± 52	70 ± 63	16
50	231 ± 135	124 ± 167	185 ± 202	181 ± 195	158 ± 168	134 ± 126	107 ± 88	117 ± 114	103 ± 112	82 ± 77	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	59-141	45-155	37-163	60-140	48-152	56-144	47-153	57-143	58-142	63-137
1	48-112	45-98	52-107	46-92	50-113	62-114	37-89	52-115	65-130	53-113
5	55-152	38-147	47-152	46-84	49-86	54-103	47-106	44-134	51-107	46-96
10	68-149	40-131	44-93	41-82	43-78	55-112	42-68	42-88	41-98	49-82
25	85-203	70-128	80-192	62-111	60-104	59-108	47-91	63-139	46-98	38-101
50	164-299	40-207	84-286	84-279	74-242	71-197	63-151	60-174	47-159	44-121

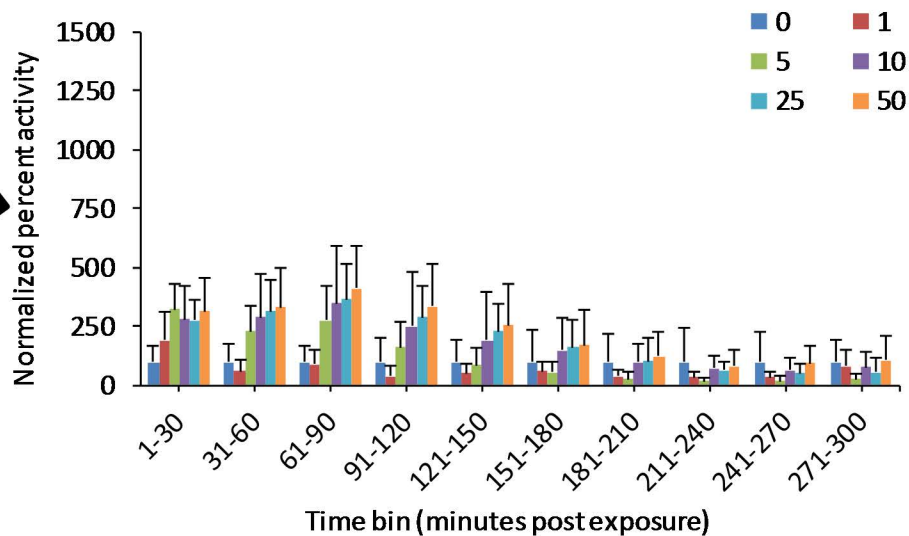
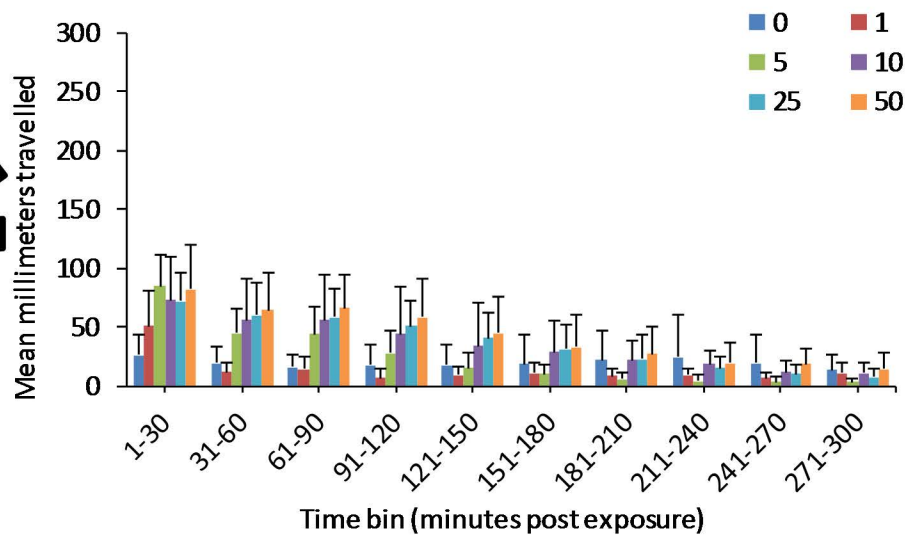
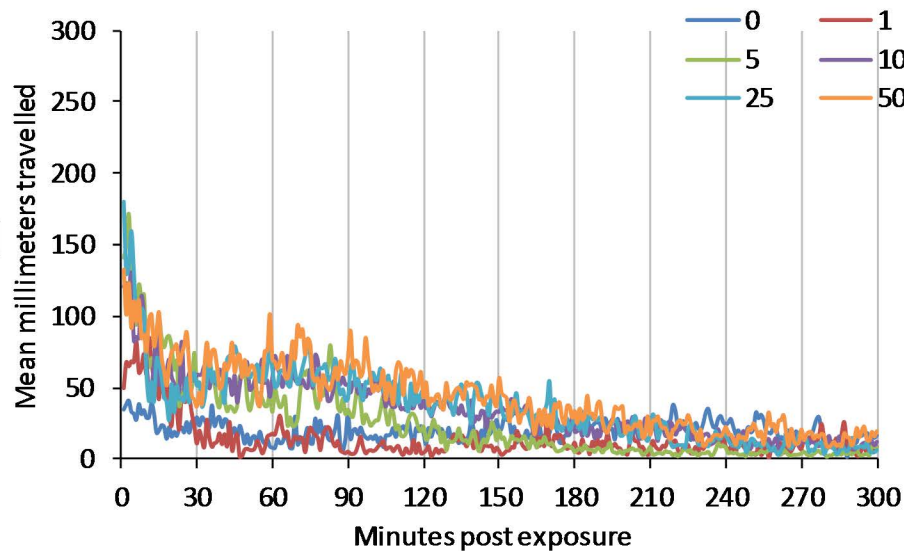
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu$ M]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.959	1.000	1.000	0.957	1.000	1.000	0.970	1.000	1.000	0.996
5	1.000	1.000	0.995	0.968	1.000	0.999	1.000	1.000	1.000	0.868
10	0.989	1.000	1.000	0.889	0.994	1.000	0.992	0.989	0.957	0.946
25	0.494	0.818	0.329	1.000	0.996	1.000	1.000	0.979	0.979	0.897
50	0.003	0.943	0.031	0.213	0.336	0.933	0.904	0.917	1.000	0.943

## Two-way repeated measures ANOVA, Tukey's post-hoc, $p \leq 0.05$

# CHEMICAL: Galangin



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 68	100 ± 78	100 ± 68	100 ± 101	100 ± 96	100 ± 132	100 ± 116	100 ± 147	100 ± 127	100 ± 93	16
1	193 ± 116	61 ± 45	90 ± 63	40 ± 43	52 ± 43	59 ± 44	40 ± 24	37 ± 23	36 ± 22	81 ± 68	16
5	324 ± 105	232 ± 105	274 ± 146	161 ± 109	85 ± 71	54 ± 43	26 ± 29	17 ± 19	19 ± 20	26 ± 26	16
10	279 ± 142	289 ± 180	349 ± 241	250 ± 230	192 ± 203	151 ± 138	99 ± 78	74 ± 50	63 ± 50	78 ± 69	16
25	276 ± 89	314 ± 138	367 ± 150	291 ± 128	229 ± 119	164 ± 115	104 ± 96	63 ± 40	52 ± 39	58 ± 56	16
50	314 ± 143	333 ± 165	410 ± 183	334 ± 184	253 ± 176	172 ± 147	124 ± 105	80 ± 69	94 ± 73	107 ± 103	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	66-134	61-139	66-134	50-150	52-148	34-166	42-158	27-173	37-163	54-146
1	135-251	38-83	59-122	19-62	31-74	37-81	28-52	25-49	25-47	47-115
5	271-376	179-284	202-347	107-215	49-120	32-76	11-40	8-27	9-29	13-39
10	207-350	199-379	229-470	135-365	90-293	82-220	60-138	49-100	38-89	44-112
25	231-320	245-383	292-442	227-355	170-289	106-221	55-152	43-83	33-72	30-86
50	243-386	250-415	319-502	242-425	165-341	98-245	72-177	46-114	57-131	55-168

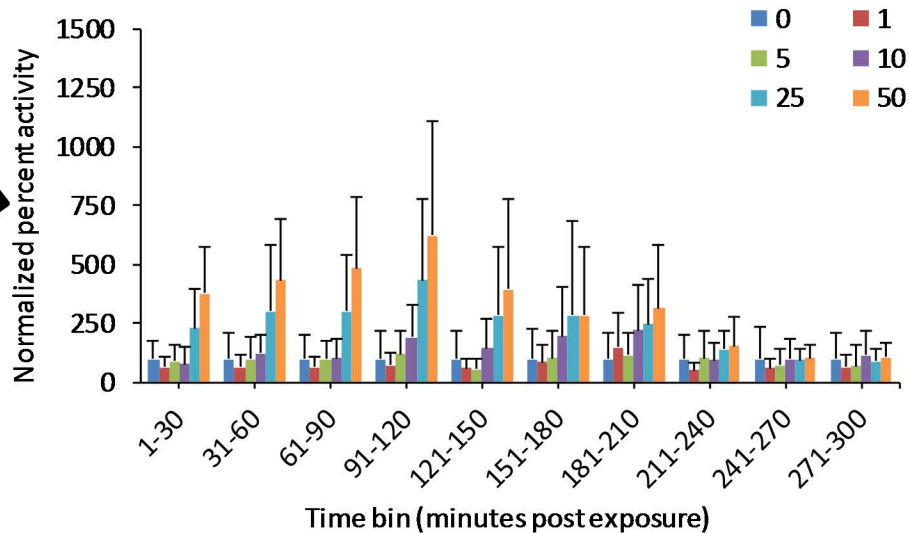
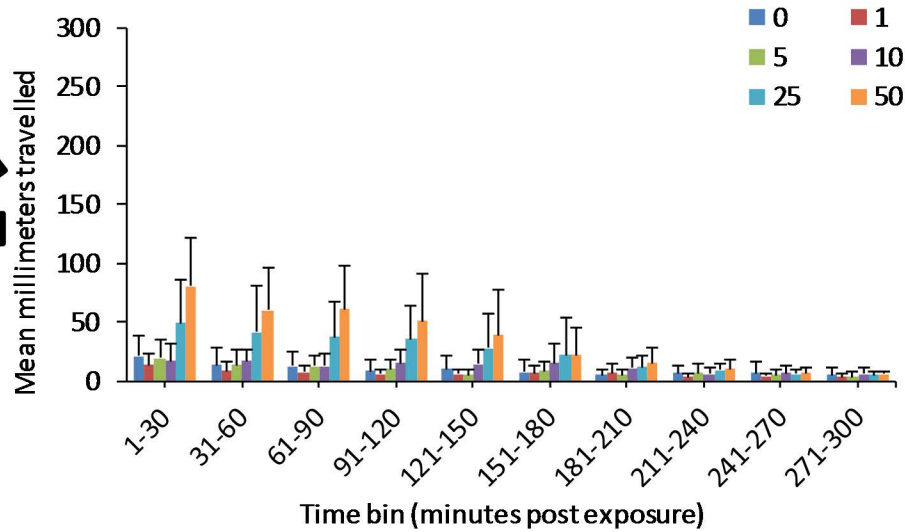
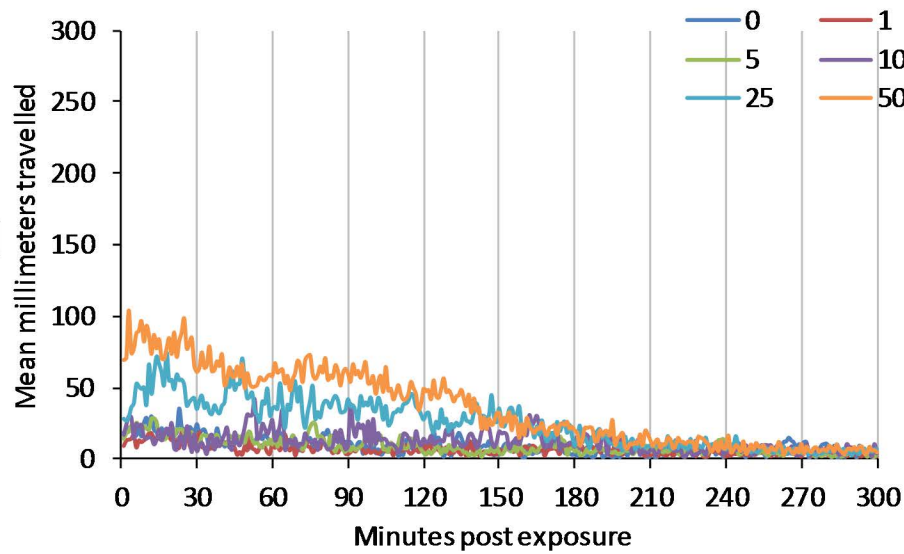
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.060	0.587	0.990	0.052	0.364	0.826	0.167	0.323	0.111	0.999
5	0.001	0.001	0.001	0.244	0.870	0.606	0.001	0.001	0.001	0.004
10	0.001	0.001	0.001	0.002	0.233	0.517	1.000	1.000	0.744	0.960
25	0.001	0.001	0.001	0.001	0.002	0.080	0.997	0.998	0.641	0.432
50	0.001	0.001	0.001	0.001	0.001	0.204	0.913	1.000	1.000	1.000

Two-way repeated measures ANOVA, Tukey's post-hoc, p ≤ 0.05

# CHEMICAL: Genistein



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 80	100 ± 107	100 ± 100	100 ± 120	100 ± 122	100 ± 131	100 ± 114	100 ± 104	100 ± 135	100 ± 114	16
1	63 ± 49	63 ± 53	63 ± 44	73 ± 51	59 ± 44	86 ± 76	149 ± 151	53 ± 33	59 ± 38	64 ± 51	16
5	91 ± 69	97 ± 99	99 ± 80	120 ± 99	55 ± 48	104 ± 117	115 ± 95	103 ± 116	72 ± 73	69 ± 94	16
10	78 ± 70	124 ± 75	103 ± 79	190 ± 138	145 ± 124	196 ± 211	223 ± 187	94 ± 78	99 ± 89	115 ± 106	16
25	228 ± 171	304 ± 279	301 ± 242	431 ± 345	283 ± 291	286 ± 399	245 ± 197	140 ± 77	92 ± 54	90 ± 57	16
50	376 ± 195	434 ± 259	484 ± 301	621 ± 486	395 ± 383	285 ± 287	313 ± 269	152 ± 125	102 ± 61	109 ± 59	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	60-140	47-153	50-150	40-160	39-161	34-166	43-157	48-152	33-167	43-157
1	39-88	36-89	41-85	47-99	37-81	48-124	73-224	37-70	40-78	39-90
5	57-126	48-147	59-139	71-170	31-79	46-162	67-162	45-161	36-109	22-116
10	43-113	87-162	64-142	121-259	83-207	91-302	129-316	55-133	55-144	62-168
25	142-313	164-443	180-422	258-603	138-429	87-486	147-343	102-179	66-119	61-118
50	279-473	304-564	334-635	378-865	203-587	142-429	179-448	89-215	72-133	79-138

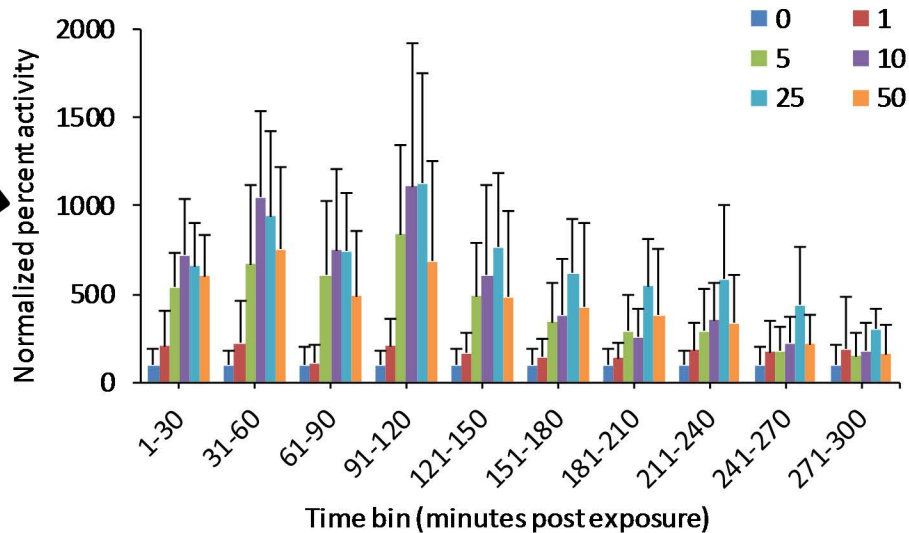
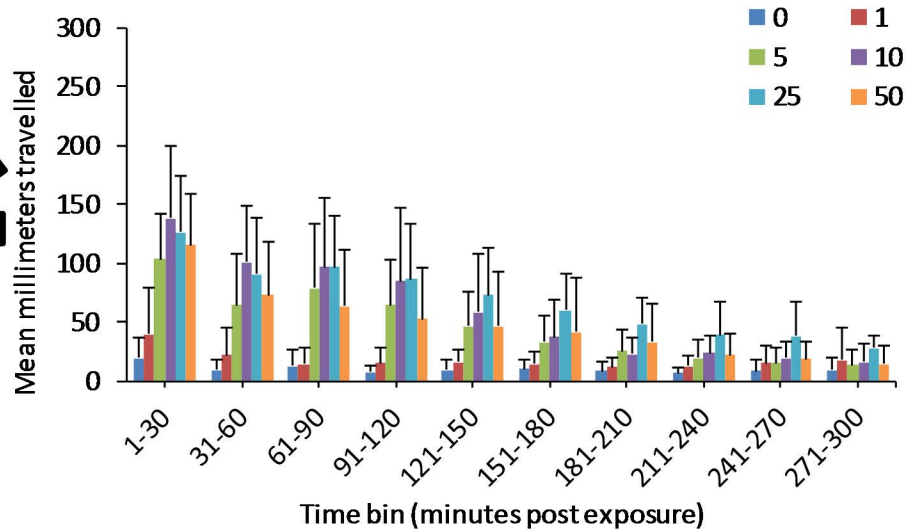
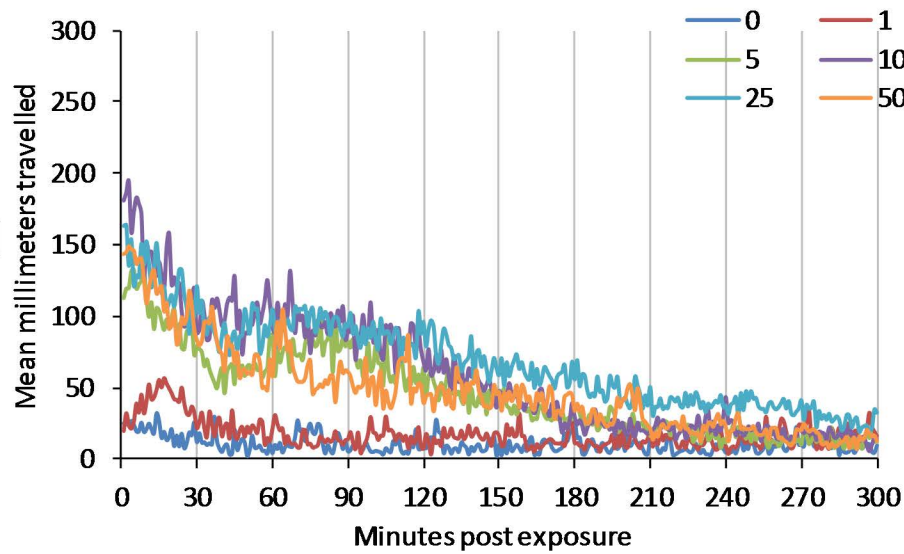
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.941	0.977	0.982	1.000	0.991	1.000	0.831	0.847	0.999	0.961
5	1.000	1.000	1.000	0.816	0.874	1.000	0.980	0.999	0.999	0.657
10	0.983	0.527	1.000	0.021	0.463	0.126	0.322	1.000	0.998	1.000
25	0.046	0.010	0.004	0.001	0.003	0.007	0.023	0.356	0.849	1.000
50	0.001	0.001	0.001	0.001	0.001	0.003	0.002	0.561	0.789	0.948

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Kaempferol



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 93	100 ± 84	100 ± 100	100 ± 77	100 ± 87	100 ± 92	100 ± 85	100 ± 78	100 ± 104	100 ± 116	16
1	206 ± 202	224 ± 238	111 ± 102	204 ± 160	166 ± 120	145 ± 104	137 ± 92	184 ± 148	172 ± 180	190 ± 289	16
5	536 ± 200	665 ± 448	604 ± 420	839 ± 509	486 ± 299	341 ± 220	291 ± 202	287 ± 237	175 ± 143	149 ± 130	16
10	719 ± 318	1047 ± 487	746 ± 456	1105 ± 812	608 ± 514	381 ± 320	258 ± 156	349 ± 219	219 ± 157	175 ± 163	16
25	657 ± 245	938 ± 487	742 ± 333	123 ± 624	763 ± 421	615 ± 310	543 ± 267	584 ± 419	436 ± 333	302 ± 115	16
50	600 ± 229	752 ± 466	489 ± 368	686 ± 566	482 ± 491	423 ± 476	378 ± 373	334 ± 272	217 ± 160	157 ± 166	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	54-146	58-142	50-150	62-138	56-144	54-146	57-143	61-139	48-152	42-158
1	104-307	105-343	60-162	124-284	106-226	93-197	91-183	110-258	82-262	46-334
5	436-635	441-889	394-814	585-1093	336-635	231-451	190-391	169-406	103-246	84-214
10	560-878	804-1291	518-974	699-1511	351-865	221-541	180-336	240-459	141-297	93-256
25	535-780	695-1182	576-909	811-1434	552-973	460-770	409-676	375-794	270-603	244-359
50	486-714	519-985	305-673	403-969	237-727	185-662	191-564	198-470	137-297	74-240

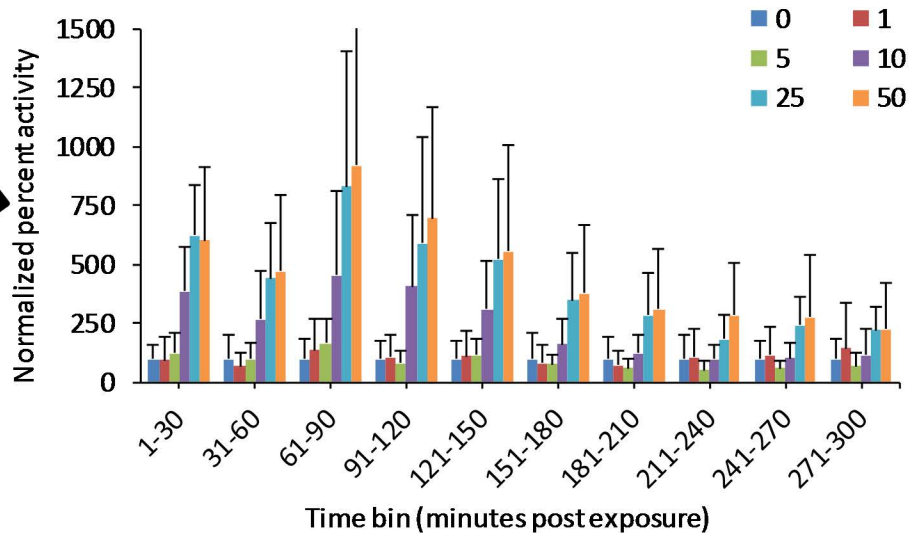
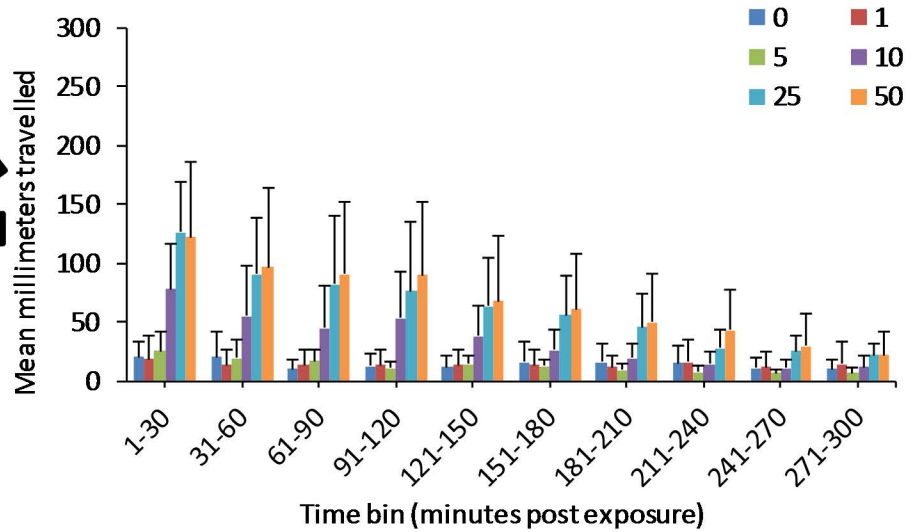
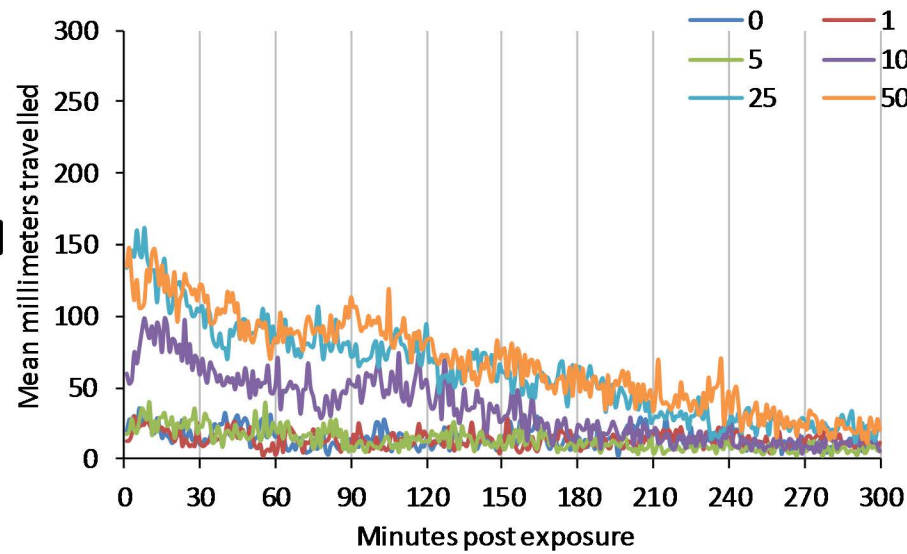
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.070	0.084	0.990	0.213	0.489	0.740	0.916	0.434	0.596	0.709
5	0.001	0.001	0.001	0.001	0.001	0.001	0.004	0.009	0.318	0.855
10	0.001	0.001	0.001	0.001	0.001	0.001	0.013	0.001	0.024	0.320
25	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
50	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.055	0.632

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Luteolin



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 63	100 ± 106	100 ± 87	100 ± 81	100 ± 77	100 ± 108	100 ± 95	100 ± 100	100 ± 80	100 ± 82	16
1	92 ± 99	68 ± 61	137 ± 131	105 ± 100	109 ± 111	83 ± 80	74 ± 58	107 ± 123	115 ± 124	143 ± 198	16
5	125 ± 84	96 ± 76	167 ± 106	82 ± 50	117 ± 65	77 ± 39	61 ± 36	51 ± 38	61 ± 34	70 ± 52	16
10	384 ± 191	269 ± 204	455 ± 357	408 ± 299	312 ± 207	161 ± 107	122 ± 77	96 ± 65	101 ± 64	117 ± 109	16
25	623 ± 215	441 ± 232	831 ± 577	588 ± 450	521 ± 344	347 ± 205	286 ± 182	181 ± 104	241 ± 123	219 ± 104	16
50	603 ± 314	472 ± 324	918 ± 612	693 ± 476	558 ± 447	378 ± 293	311 ± 258	284 ± 219	275 ± 266	226 ± 193	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	68-132	47-153	57-143	60-140	61-139	46-154	53-147	50-150	60-140	59-141
1	43-142	37-99	72-203	55-155	53-165	43-123	45-103	46-169	53-177	44-243
5	83-167	58-134	114-220	57-107	84-149	57-96	43-79	32-70	44-78	43-96
10	289-480	167-372	277-634	259-558	208-415	107-215	84-161	64-129	69-132	63-171
25	515-730	325-557	543-1119	363-813	348-693	245-449	195-377	129-233	179-303	168-271
50	446-760	310-634	612-1224	456-931	334-781	231-524	182-440	175-394	142-408	130-323

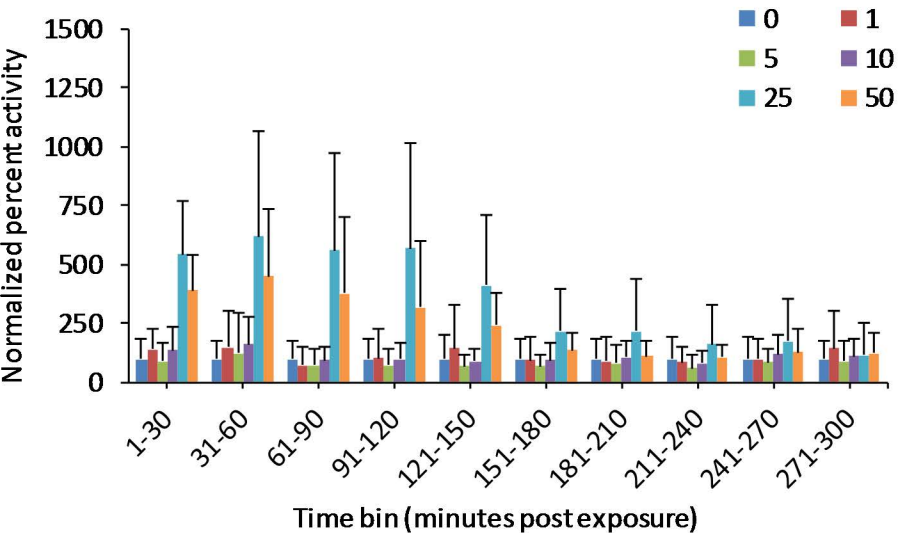
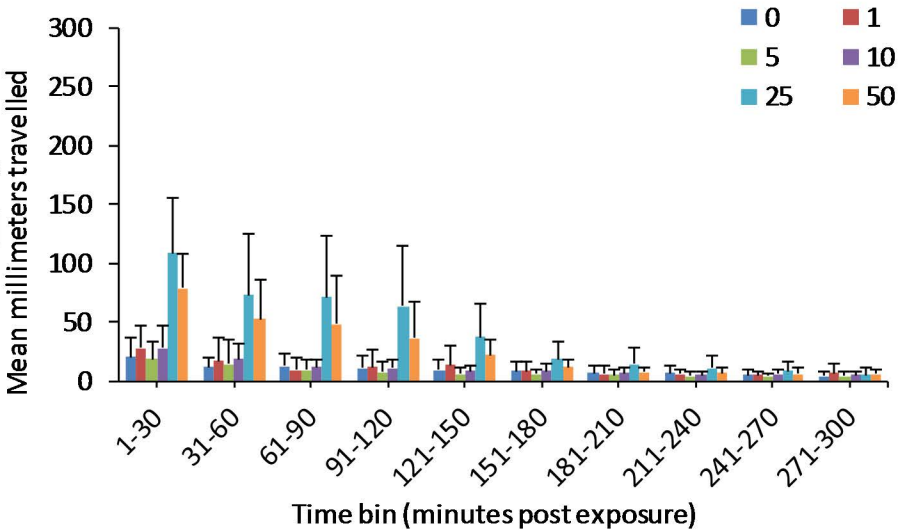
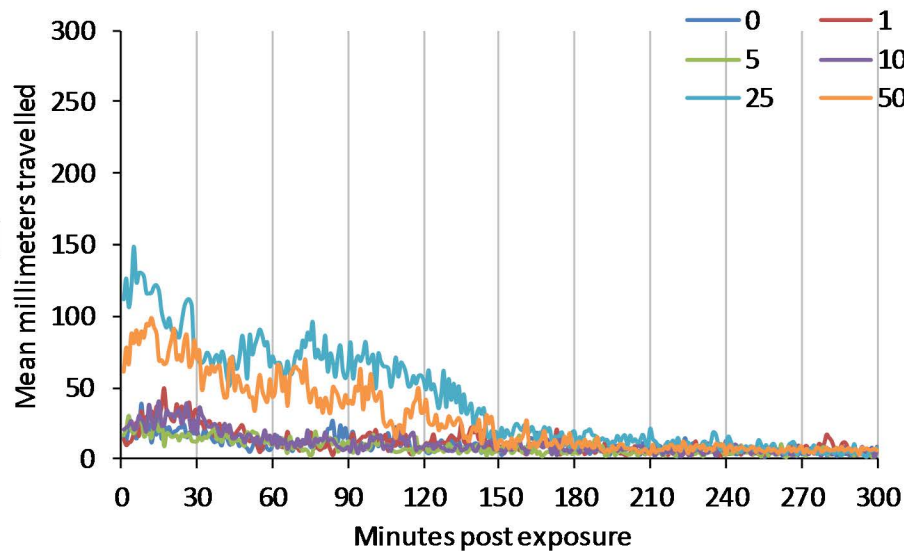
## 95% confidence interval

## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.937	0.991	0.917	1.000	1.000	0.998	0.999	1.000	0.999	1.000
5	0.763	0.940	0.205	1.000	0.905	0.999	0.978	0.764	0.986	0.936
10	0.001	0.001	0.001	0.001	0.001	0.096	0.531	0.988	0.993	0.996
25	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.035	0.002	0.026
50	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.087

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

**CHEMICAL: Morin**



**Normalized percent activity**

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 83	100 ± 75	100 ± 81	100 ± 88	100 ± 101	100 ± 89	100 ± 86	100 ± 90	100 ± 91	100 ± 74	16
1	141 ± 90	147 ± 160	74 ± 78	103 ± 126	147 ± 179	94 ± 103	89 ± 103	86 ± 63	99 ± 87	145 ± 160	16
5	92 ± 76	123 ± 173	75 ± 64	71 ± 72	67 ± 50	67 ± 52	80 ± 76	62 ± 56	86 ± 56	92 ± 81	16
10	138 ± 98	160 ± 117	92 ± 58	100 ± 66	92 ± 51	96 ± 70	106 ± 74	81 ± 51	120 ± 84	112 ± 73	16
25	543 ± 231	617 ± 449	558 ± 445	567 ± 445	411 ± 301	215 ± 179	218 ± 222	160 ± 170	175 ± 181	115 ± 137	16
50	392 ± 145	451 ± 283	379 ± 323	320 ± 278	240 ± 138	135 ± 76	110 ± 69	107 ± 56	127 ± 101	122 ± 85	16

**Mean ± standard deviation**

**Normalized percent activity**

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	58-142	62-138	60-140	56-144	49-151	56-144	57-143	55-145	55-145	63-137
1	96-186	67-227	35-113	40-166	57-236	43-145	38-141	54-118	56-143	65-225
5	54-130	37-210	43-107	35-107	43-92	41-93	42-118	34-90	58-114	51-132
10	89-187	102-219	63-121	67-133	66-117	60-131	69-143	55-106	78-162	75-149
25	427-658	393-842	351-766	344-789	261-562	126-305	108-329	75-245	85-265	47-184
50	320-465	309-592	217-540	181-459	171-310	97-173	75-144	78-135	77-178	79-164

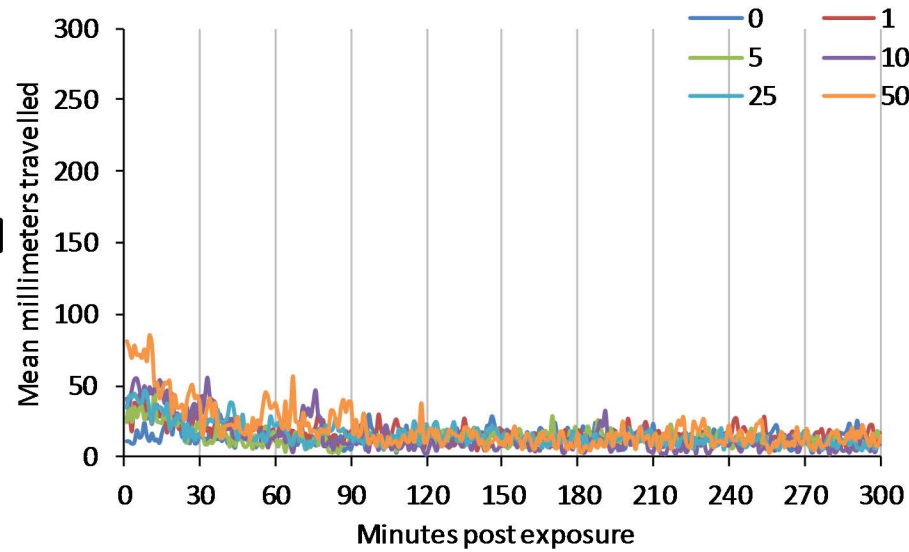
**95% confidence interval**

**p-values**

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.640	1.000	0.826	1.000	0.888	0.998	1.000	1.000	1.000	0.999
5	1.000	1.000	0.889	0.913	1.000	0.919	0.979	0.873	1.000	0.993
10	0.725	0.603	1.000	0.989	0.925	1.000	0.992	1.000	0.945	0.992
25	0.001	0.001	0.001	0.002	0.002	0.693	0.934	0.914	0.970	0.992
50	0.001	0.001	0.001	0.001	0.001	0.656	0.418	0.950	0.942	0.996

**Two-way repeated measures ANOVA, Tukey's post-hoc, p ≤ 0.05**

# CHEMICAL: Myricetin



Normalized percent activity		Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 76	100 ± 66	100 ± 78	100 ± 62	100 ± 82	100 ± 83	100 ± 82	100 ± 76	100 ± 78	100 ± 70	16
1	169 ± 85	151 ± 129	125 ± 124	119 ± 76	85 ± 62	82 ± 57	99 ± 86	96 ± 69	124 ± 95	99 ± 71	16
5	152 ± 130	94 ± 59	74 ± 45	93 ± 41	85 ± 75	83 ± 66	95 ± 90	84 ± 74	98 ± 102	81 ± 63	16
10	240 ± 222	172 ± 162	139 ± 157	80 ± 94	55 ± 37	62 ± 49	84 ± 104	52 ± 40	78 ± 74	52 ± 39	16
25	173 ± 122	162 ± 139	123 ± 139	98 ± 86	95 ± 83	78 ± 67	83 ± 64	74 ± 51	86 ± 62	59 ± 34	16
50	319 ± 169	193 ± 195	206 ± 187	104 ± 72	80 ± 99	74 ± 99	73 ± 77	101 ± 144	100 ± 109	87 ± 117	16

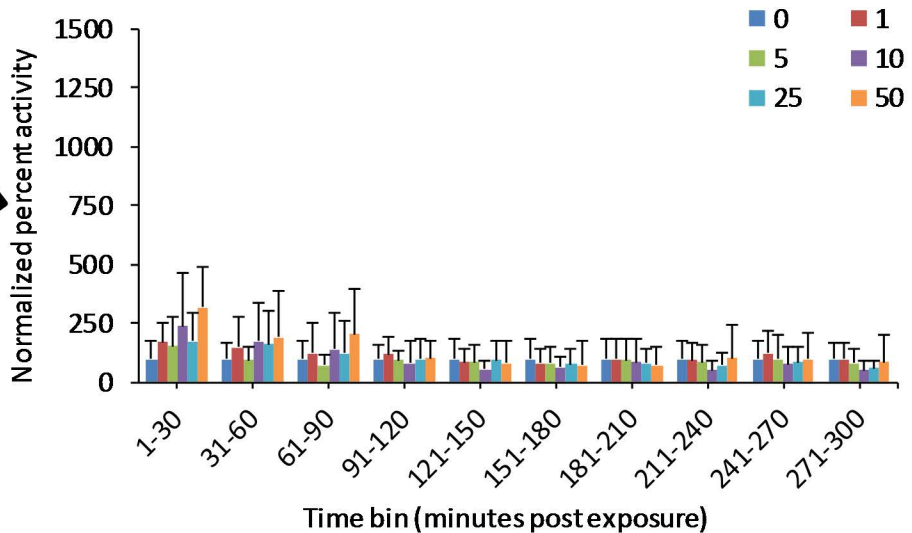
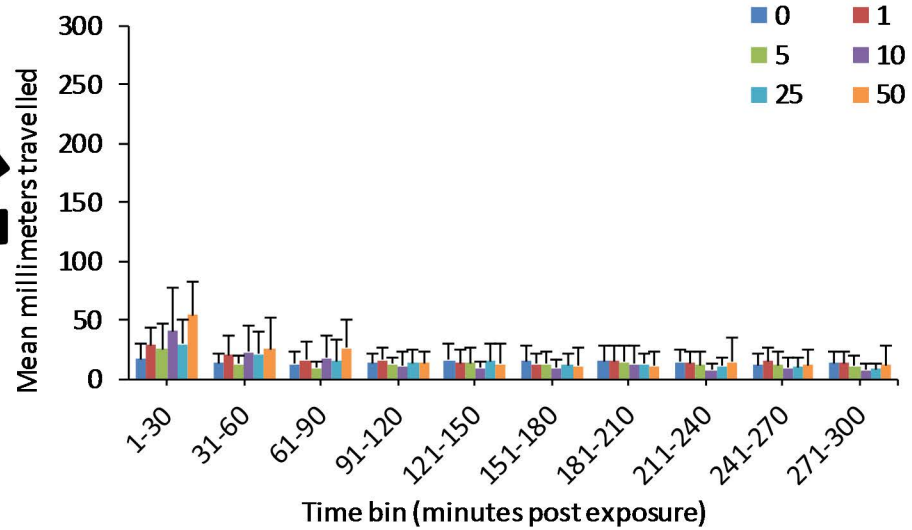
Mean ± standard deviation

Normalized percent activity		Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	62-138	67-133	61-139	69-131	59-141	59-141	59-141	62-138	61-139	65-135	
1	127-212	86-216	63-187	81-157	54-116	54-110	56-142	62-131	76-171	64-135	
5	88-217	65-124	51-96	72-114	47-122	50-117	50-139	47-122	48-149	50-113	
10	129-350	91-254	60-217	33-127	36-74	38-87	32-136	32-72	41-115	33-72	
25	113-234	92-231	54-193	55-142	53-137	44-112	51-115	49-100	55-118	42-76	
50	235-403	96-290	112-299	68-140	30-129	25-124	34-111	29-173	46-154	28-145	

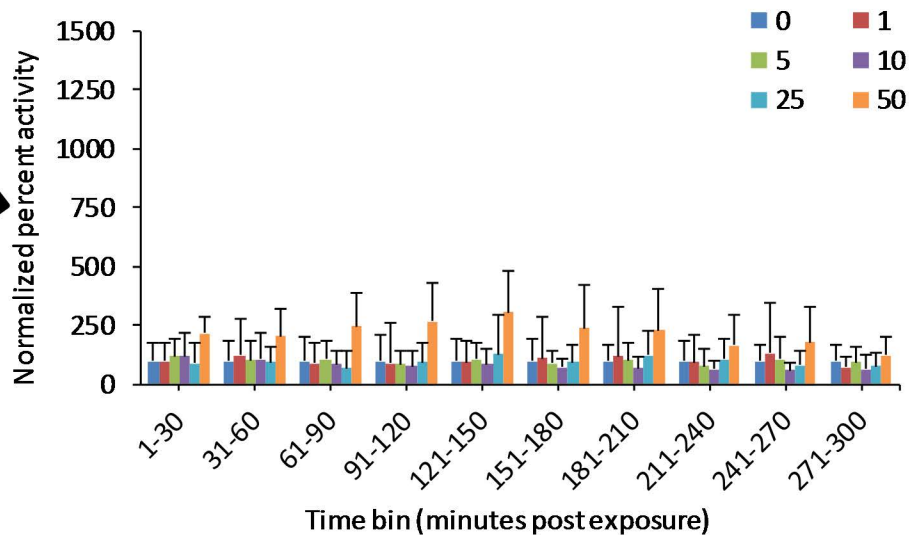
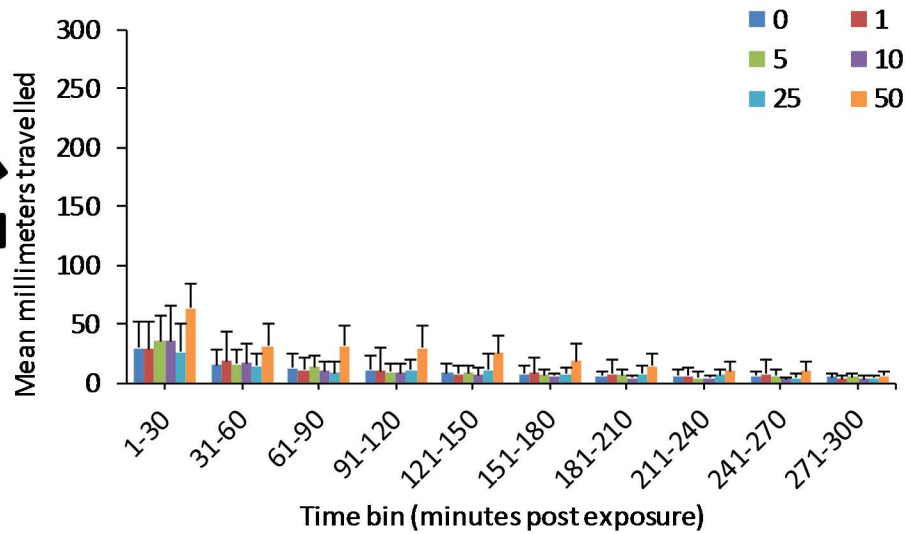
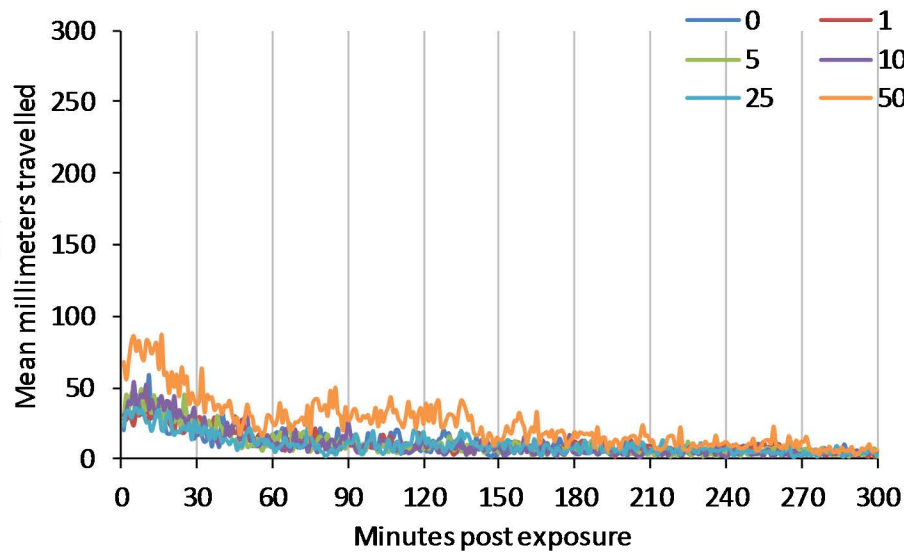
95% confidence interval

p-values		Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
1	0.140	0.865	0.980	0.985	1.000	1.000	1.000	0.998	0.976	1.000	
5	0.605	1.000	0.997	1.000	0.998	0.999	1.000	1.000	1.000	0.997	
10	0.238	0.996	1.000	0.617	0.600	0.716	0.788	0.404	0.816	0.262	
25	0.608	0.927	0.999	0.999	0.999	0.977	0.995	0.994	0.996	0.740	
50	0.001	0.765	0.101	1.000	0.901	0.722	0.828	0.997	1.000	0.767	

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Naringenin



## Normalized percent activity

[μM]	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
0	100 ± 75	100 ± 82	100 ± 102	100 ± 107	100 ± 92	100 ± 90	100 ± 67	100 ± 84	100 ± 70	100 ± 65	16
1	98 ± 77	123 ± 157	90 ± 86	91 ± 167	93 ± 94	113 ± 172	120 ± 213	95 ± 115	133 ± 217	73 ± 49	16
5	119 ± 72	104 ± 79	109 ± 77	86 ± 57	107 ± 74	91 ± 48	104 ± 73	77 ± 75	106 ± 100	95 ± 63	16
10	121 ± 100	108 ± 109	84 ± 61	75 ± 67	87 ± 66	71 ± 40	69 ± 45	65 ± 39	60 ± 32	65 ± 57	16
25	88 ± 85	93 ± 70	69 ± 72	94 ± 87	130 ± 164	94 ± 77	125 ± 101	106 ± 86	81 ± 63	77 ± 58	16
50	216 ± 72	205 ± 117	247 ± 139	266 ± 165	305 ± 175	237 ± 182	230 ± 174	168 ± 124	178 ± 149	123 ± 81	16

## Mean ± standard deviation

## Normalized percent activity

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	63-137	59-141	49-151	47-153	54-146	55-145	67-133	58-142	65-135	67-133
1	60-136	45-202	47-134	8-175	46-141	27-199	13-226	38-152	24-241	48-97
5	84-155	65-144	71-147	57-114	70-144	67-115	67-141	39-114	55-156	64-127
10	71-171	54-163	53-114	42-109	54-120	51-91	47-91	46-85	44-77	36-93
25	46-131	58-128	33-105	51-137	48-112	55-133	74-175	63-149	50-112	48-106
50	180-252	146-264	177-316	183-348	217-392	146-328	143-317	106-229	104-253	82-163

## 95% confidence interval

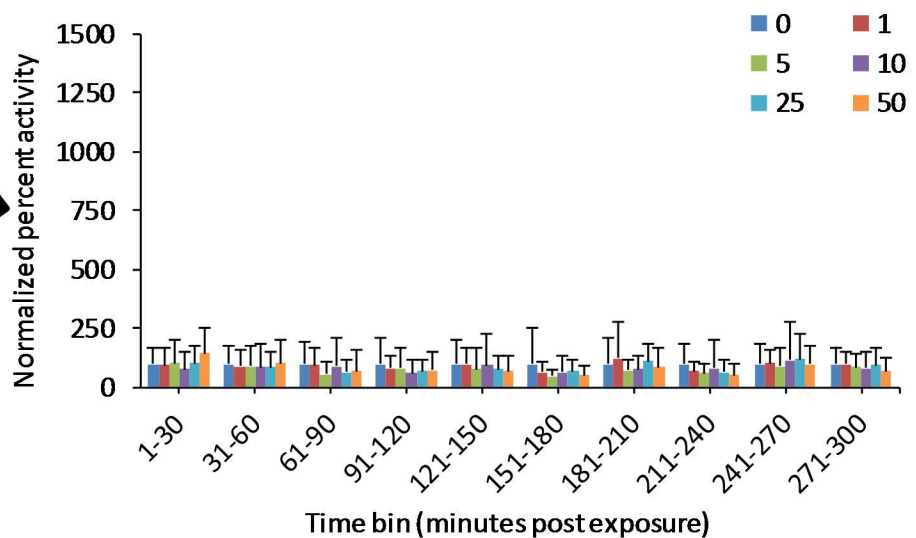
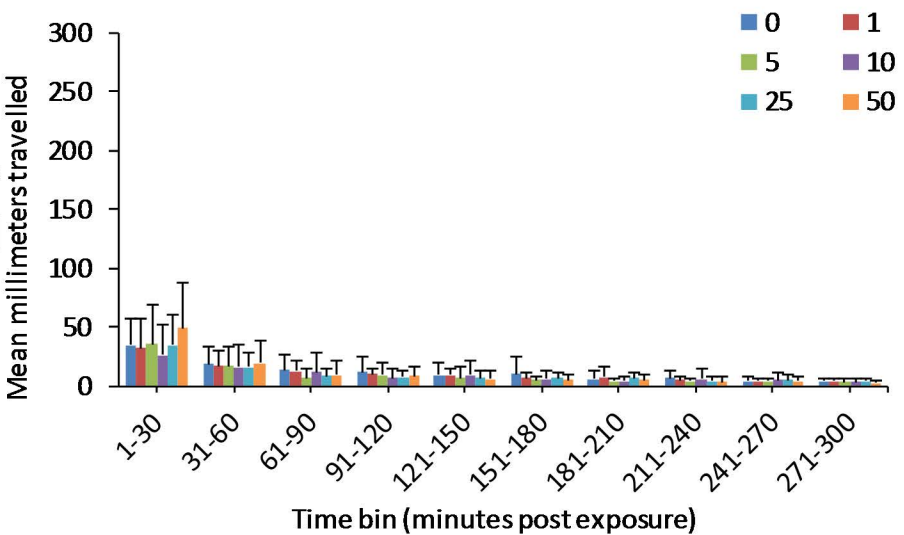
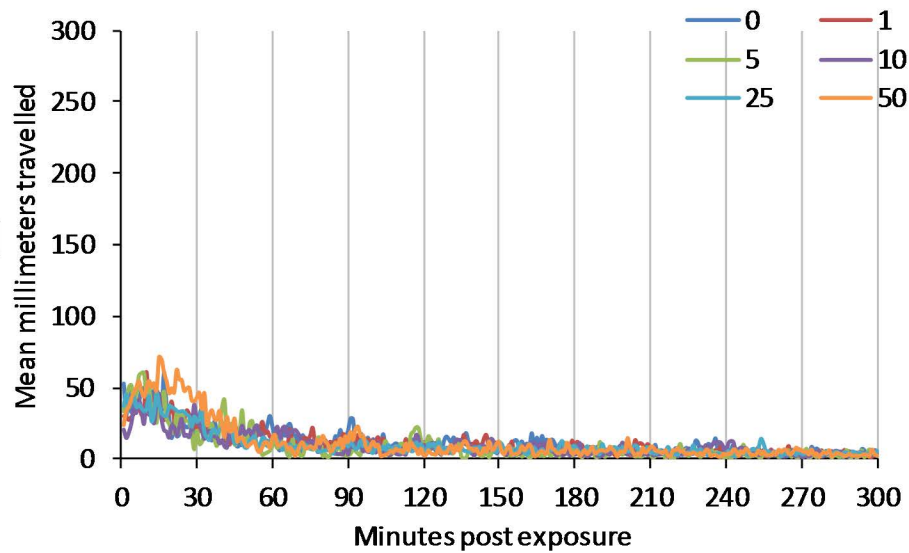
## p-values

[μM]	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	1.000	0.957	0.992	0.839	0.986	1.000	0.999	0.999	1.000	0.944
5	0.861	1.000	0.996	1.000	0.994	1.000	1.000	0.820	1.000	1.000
10	0.961	1.000	1.000	0.981	1.000	0.999	0.948	0.925	0.903	0.565
25	0.953	0.994	0.568	1.000	1.000	1.000	0.993	1.000	0.986	0.949
50	0.007	0.066	0.005	0.001	0.001	0.084	0.060	0.444	0.385	0.986

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$



# CHEMICAL: Puerarin



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 68	100 ± 76	100 ± 97	100 ± 107	100 ± 105	100 ± 156	100 ± 110	100 ± 85	100 ± 89	100 ± 70	16
1	94 ± 72	91 ± 67	94 ± 74	83 ± 49	100 ± 64	66 ± 44	124 ± 152	71 ± 41	102 ± 59	100 ± 51	16
5	103 ± 96	88 ± 87	54 ± 54	80 ± 88	76 ± 90	47 ± 32	73 ± 46	60 ± 41	90 ± 74	87 ± 55	16
10	77 ± 73	85 ± 102	91 ± 119	60 ± 60	94 ± 134	62 ± 71	76 ± 60	82 ± 123	117 ± 165	83 ± 66	16
25	101 ± 76	85 ± 63	66 ± 50	68 ± 47	76 ± 56	70 ± 47	109 ± 77	64 ± 51	118 ± 111	96 ± 75	16
50	143 ± 113	104 ± 97	70 ± 88	71 ± 76	67 ± 70	54 ± 42	86 ± 79	53 ± 52	98 ± 80	68 ± 61	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	66-134	62-138	51-149	47-153	48-152	22-178	45-155	57-143	56-144	65-135
1	58-130	58-125	57-131	59-108	68-132	43-88	49-200	50-91	72-131	74-126
5	55-151	45-132	27-81	36-124	31-121	31-63	50-96	40-80	53-127	60-114
10	40-113	34-136	31-150	30-90	27-161	27-98	46-106	21-143	34-199	50-116
25	63-140	54-117	41-90	44-92	48-104	47-93	71-148	38-90	62-173	58-134
50	87-199	55-152	26-114	33-109	32-102	33-75	46-126	27-79	58-138	38-99

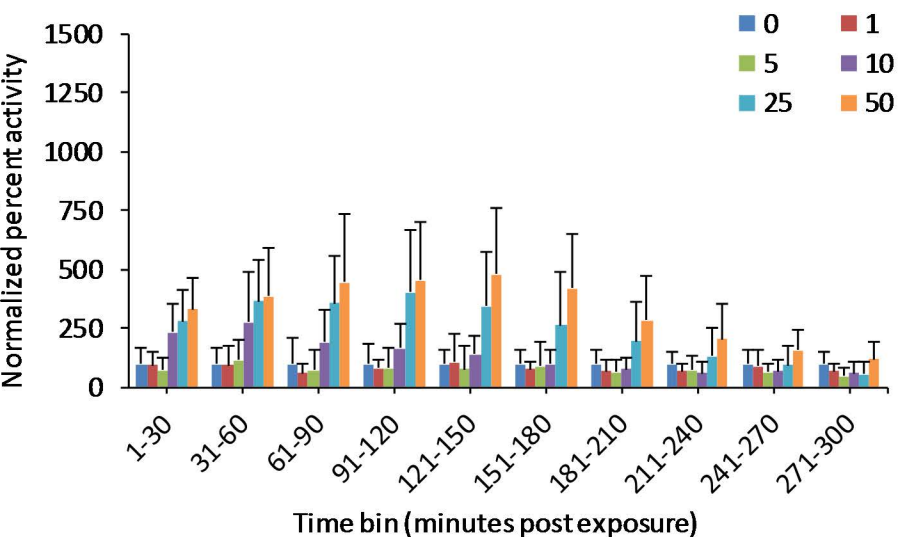
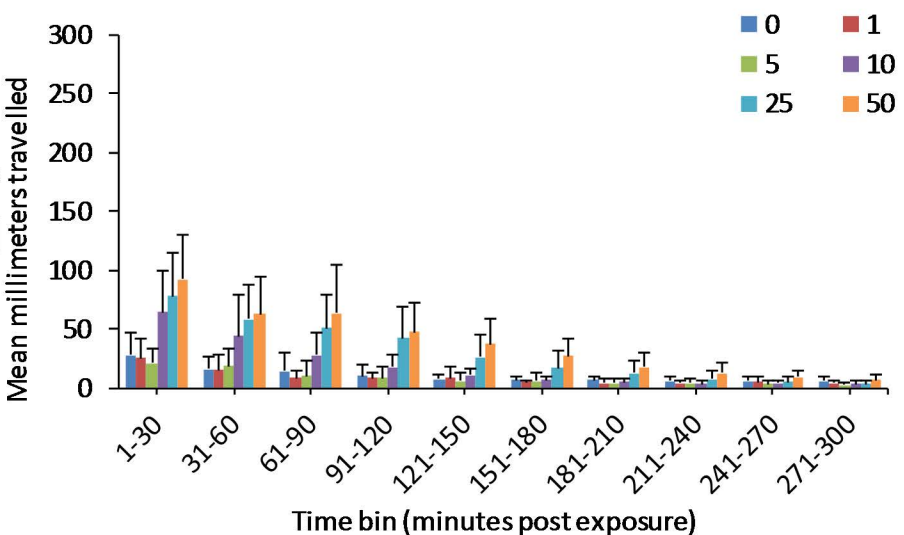
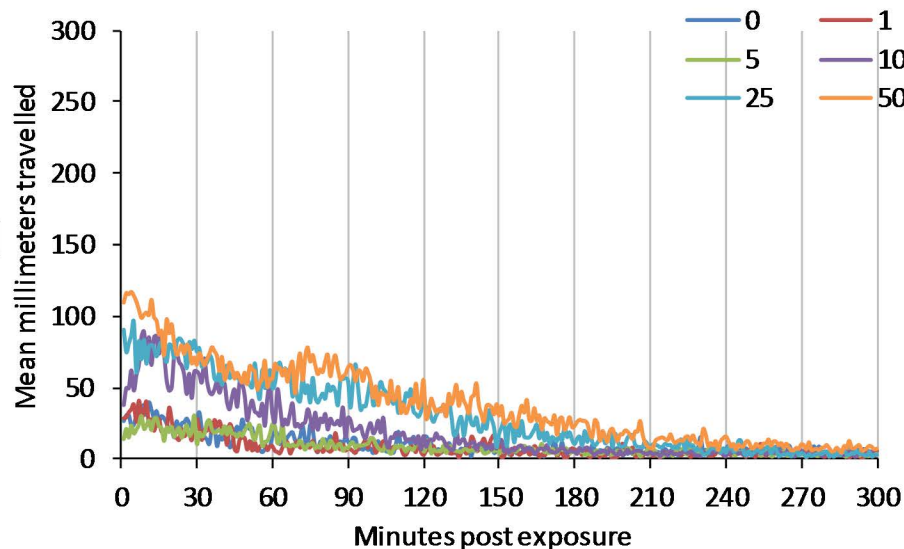
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	1.000	1.000	1.000	1.000	0.988	0.997	0.945	0.988	0.993	1.000
5	1.000	0.999	0.486	0.993	0.945	0.731	1.000	0.773	1.000	1.000
10	0.899	0.514	0.629	0.908	0.957	0.926	1.000	0.880	1.000	0.990
25	1.000	1.000	0.694	1.000	0.997	1.000	0.984	0.721	0.999	0.999
50	1.000	0.899	0.215	0.777	0.660	0.752	1.000	0.225	1.000	0.586

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Quercetin



## Normalized percent activity

	Time bin (minutes post exposure)										
[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 68	100 ± 71	100 ± 114	100 ± 89	100 ± 57	100 ± 59	100 ± 64	100 ± 53	100 ± 63	100 ± 55	16
1	93 ± 58	94 ± 84	61 ± 39	80 ± 39	107 ± 120	76 ± 32	70 ± 47	70 ± 33	92 ± 66	69 ± 31	16
5	75 ± 48	116 ± 87	71 ± 86	81 ± 89	76 ± 101	90 ± 100	64 ± 52	72 ± 60	63 ± 39	48 ± 32	16
10	233 ± 123	276 ± 214	193 ± 136	167 ± 106	141 ± 81	99 ± 64	75 ± 53	61 ± 50	69 ± 47	60 ± 52	16
25	279 ± 130	364 ± 178	355 ± 203	403 ± 264	343 ± 234	265 ± 222	194 ± 169	133 ± 119	93 ± 81	57 ± 56	16
50	332 ± 135	387 ± 201	444 ± 292	454 ± 244	479 ± 283	419 ± 232	283 ± 189	205 ± 148	156 ± 92	122 ± 76	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	66-134	65-135	43-167	56-144	71-129	71-129	68-132	73-127	69-131	72-128
1	64-122	52-137	41-81	61-100	47-167	60-92	47-94	53-87	59-125	54-85
5	51-99	72-159	28-115	36-125	25-126	40-140	37-90	42-102	44-83	33-64
10	171-294	169-383	125-261	114-220	100-181	67-131	49-102	36-86	45-93	35-86
25	214-345	275-453	253-456	271-535	226-460	154-376	109-279	73-192	53-133	29-85
50	265-399	287-488	298-590	333-576	337-620	303-535	188-377	132-279	110-202	84-160

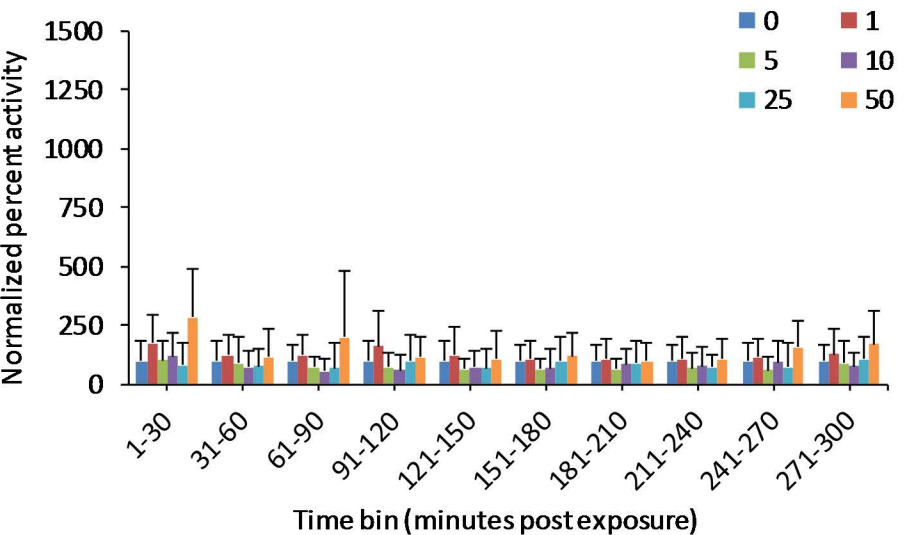
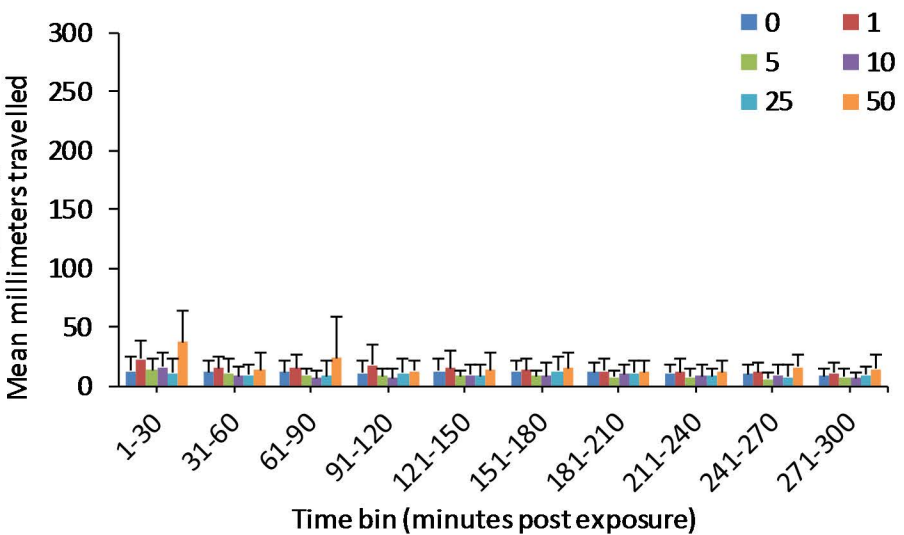
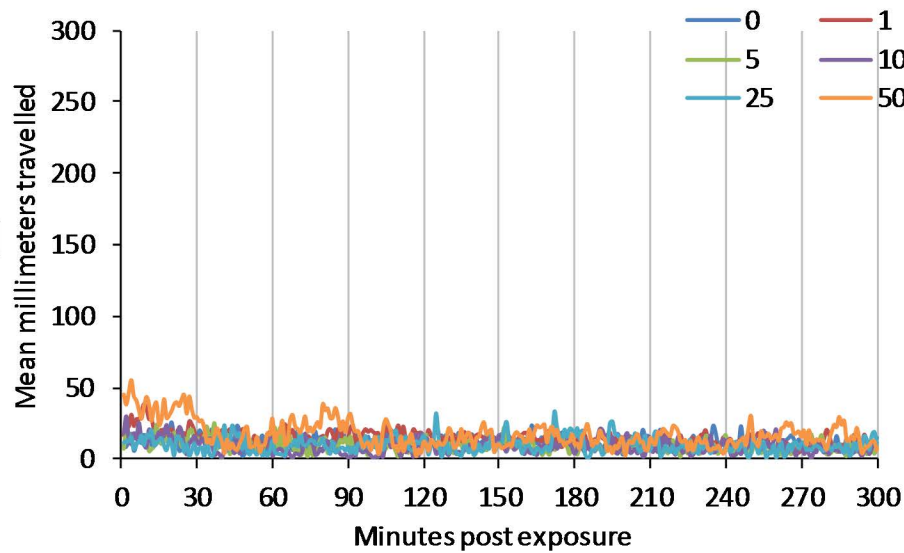
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	1.000	1.000	0.743	1.000	1.000	0.981	0.762	0.895	1.000	0.863
5	0.924	0.993	0.928	0.724	0.185	0.761	0.371	0.469	0.604	0.062
10	0.011	0.006	0.029	0.228	0.812	1.000	0.914	0.226	0.752	0.157
25	0.001	0.001	0.001	0.001	0.001	0.073	0.606	0.999	0.893	0.045
50	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.161	0.393	0.991

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Quercetin 3-β-D glucoside



## Normalized percent activity

	Time bin (minutes post exposure)										
[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 89	100 ± 82	100 ± 71	100 ± 85	100 ± 81	100 ± 69	100 ± 71	100 ± 65	100 ± 79	100 ± 72	16
1	174 ± 121	124 ± 89	124 ± 90	160 ± 151	124 ± 117	107 ± 77	107 ± 83	109 ± 93	115 ± 78	126 ± 111	16
5	104 ± 80	91 ± 107	74 ± 44	74 ± 59	65 ± 43	64 ± 41	63 ± 44	67 ± 63	61 ± 53	90 ± 92	16
10	121 ± 96	73 ± 70	54 ± 54	62 ± 66	74 ± 69	68 ± 83	85 ± 64	78 ± 82	93 ± 89	77 ± 53	16
25	83 ± 94	75 ± 75	70 ± 102	98 ± 111	68 ± 80	100 ± 100	92 ± 92	72 ± 57	71 ± 108	106 ± 93	16
50	283 ± 204	115 ± 118	198 ± 285	115 ± 84	109 ± 120	118 ± 104	97 ± 80	109 ± 85	159 ± 108	171 ± 141	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	55-145	59-141	65-135	57-143	59-141	65-135	65-135	67-133	61-139	64-136
1	114-235	80-168	80-169	84-235	65-182	68-145	65-148	62-155	76-154	71-181
5	64-144	38-145	52-96	44-104	43-86	44-85	41-85	35-99	34-87	45-136
10	73-170	38-108	27-81	29-95	39-109	27-110	53-117	37-120	49-137	50-104
25	36-130	38-113	19-121	43-154	28-108	50-150	46-138	43-100	18-125	59-152
50	181-385	56-174	56-341	73-157	49-169	66-170	57-138	66-151	105-213	101-241

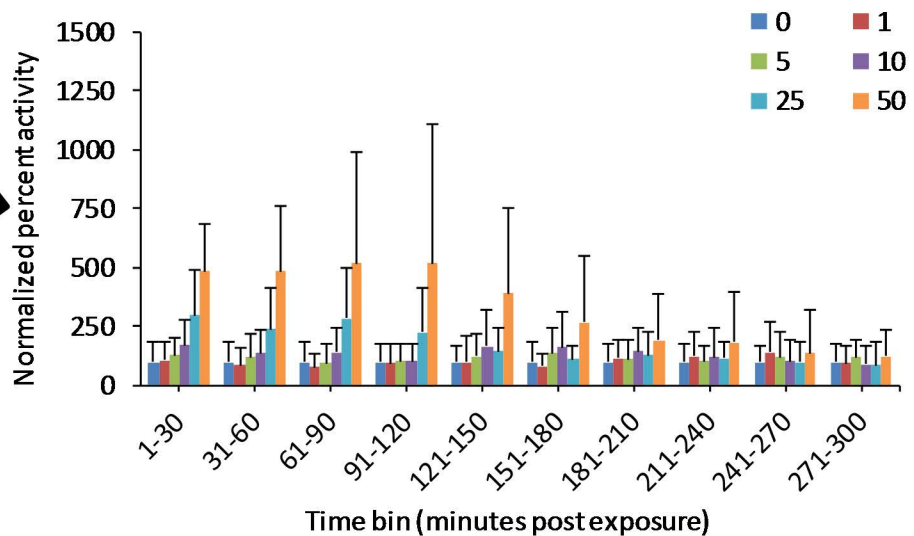
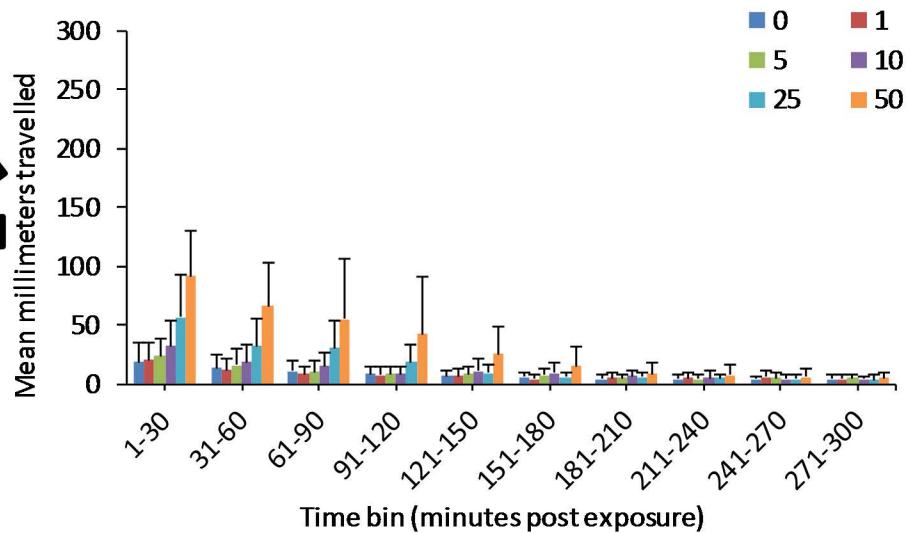
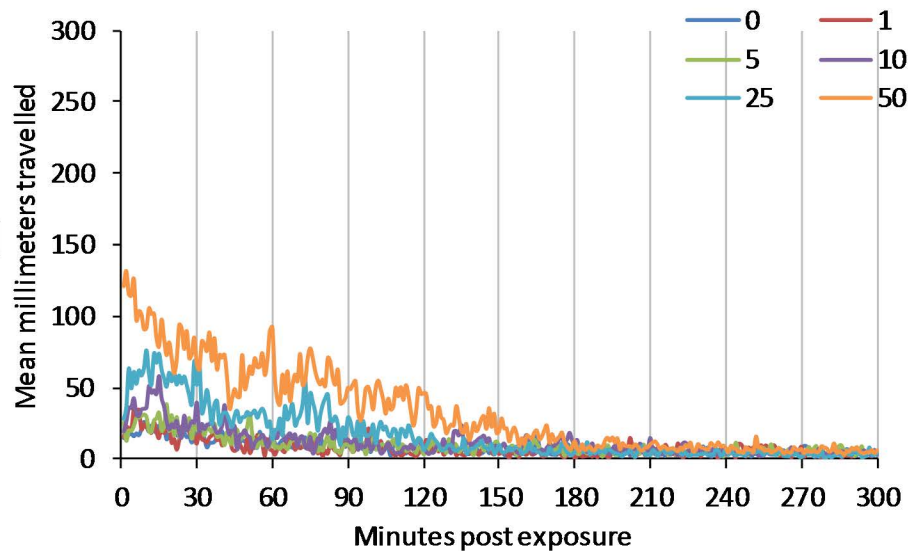
## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[μM]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.422	0.996	0.993	0.901	0.983	1.000	1.000	1.000	0.974	0.998
5	1.000	0.997	0.964	0.977	0.955	0.815	0.719	0.729	0.835	0.981
10	0.999	0.817	0.093	0.388	0.955	0.361	0.974	0.794	1.000	0.955
25	0.838	0.924	0.369	0.979	0.437	0.963	0.866	0.840	0.798	1.000
50	0.010	1.000	0.981	0.999	1.000	1.000	1.000	1.000	0.600	0.953

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Resveratrol



## Normalized percent activity

	Time bin (minutes post exposure)										
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
0	100 ± 82	100 ± 89	100 ± 82	100 ± 81	100 ± 71	100 ± 81	100 ± 73	100 ± 80	100 ± 65	100 ± 80	16
1	108 ± 77	84 ± 71	78 ± 55	92 ± 83	100 ± 12	81 ± 53	113 ± 84	123 ± 108	142 ± 130	95 ± 76	16
5	127 ± 76	121 ± 98	95 ± 85	104 ± 69	126 ± 91	137 ± 106	111 ± 83	101 ± 70	119 ± 108	121 ± 75	16
10	171 ± 109	135 ± 105	142 ± 102	105 ± 69	166 ± 155	161 ± 154	144 ± 97	119 ± 126	103 ± 90	90 ± 76	16
25	299 ± 188	238 ± 173	284 ± 211	226 ± 191	145 ± 97	112 ± 56	127 ± 104	113 ± 74	99 ± 83	87 ± 94	16
50	483 ± 205	483 ± 275	516 ± 470	517 ± 588	390 ± 361	268 ± 277	190 ± 199	182 ± 213	138 ± 179	122 ± 117	16

## Mean ± standard deviation

## Normalized percent activity

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
0	59-141	55-145	59-141	60-140	65-135	59-141	64-136	60-140	68-132	60-140
1	69-146	49-120	50-105	51-134	44-156	54-107	72-155	69-177	77-207	57-133
5	89-165	72-170	52-137	70-138	80-171	83-190	70-152	66-136	65-173	83-159
10	116-225	83-187	91-193	70-139	89-244	84-238	95-192	56-183	58-148	52-128
25	205-393	152-325	179-390	130-321	96-193	84-140	75-179	76-150	58-141	40-134
50	380-586	345-620	280-751	223-811	210-571	129-407	90-289	76-289	49-228	63-180

## 95% confidence interval

## p-values

	Time bin (minutes post exposure)									
[ $\mu\text{M}$ ]	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
1	0.999	0.894	0.964	0.991	0.999	0.997	0.993	0.996	0.961	1.000
5	0.907	1.000	0.980	1.000	0.997	0.955	0.996	1.000	1.000	0.993
10	0.241	0.913	0.883	0.999	0.913	0.763	0.744	1.000	0.997	0.993
25	0.002	0.131	0.012	0.107	0.784	0.961	0.985	0.993	1.000	0.952
50	0.001	0.001	0.001	0.001	0.003	0.078	0.429	0.662	1.000	1.000

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# Pharmacological intervention studies

**3 test chemicals:**

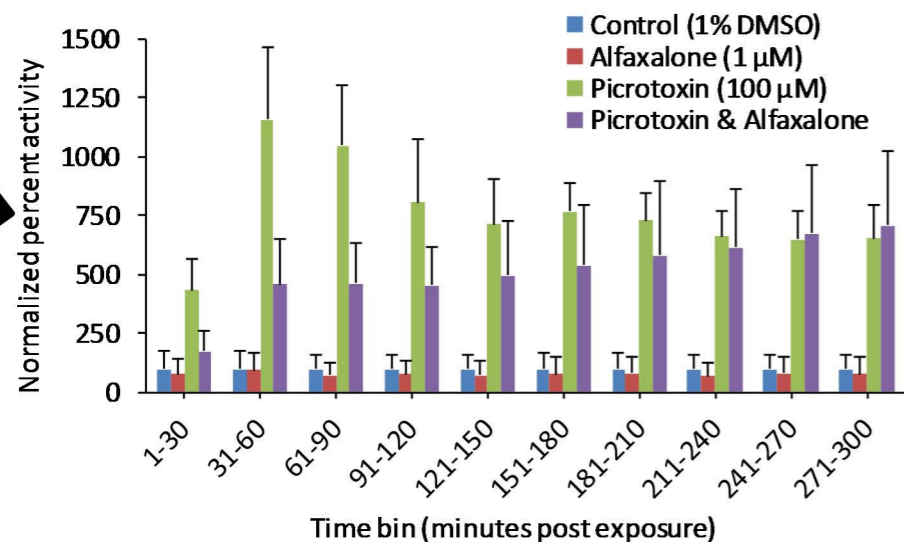
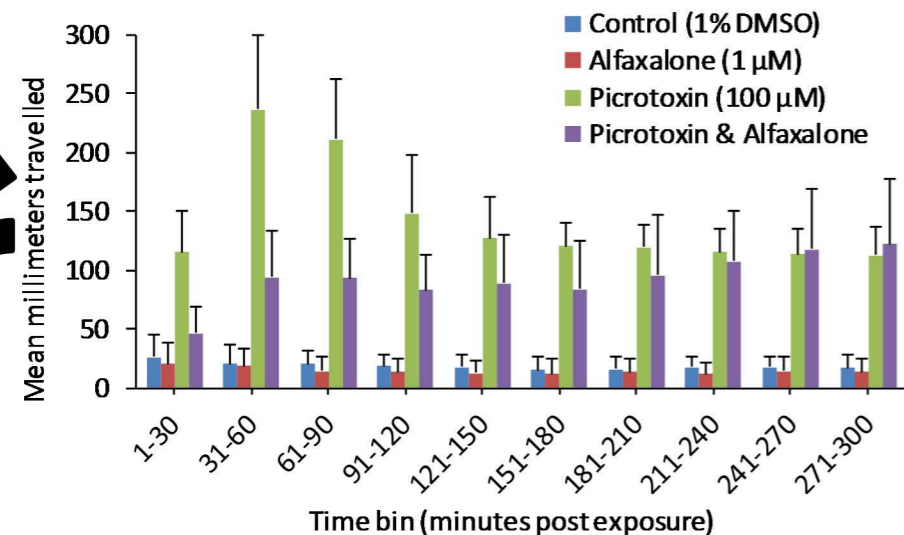
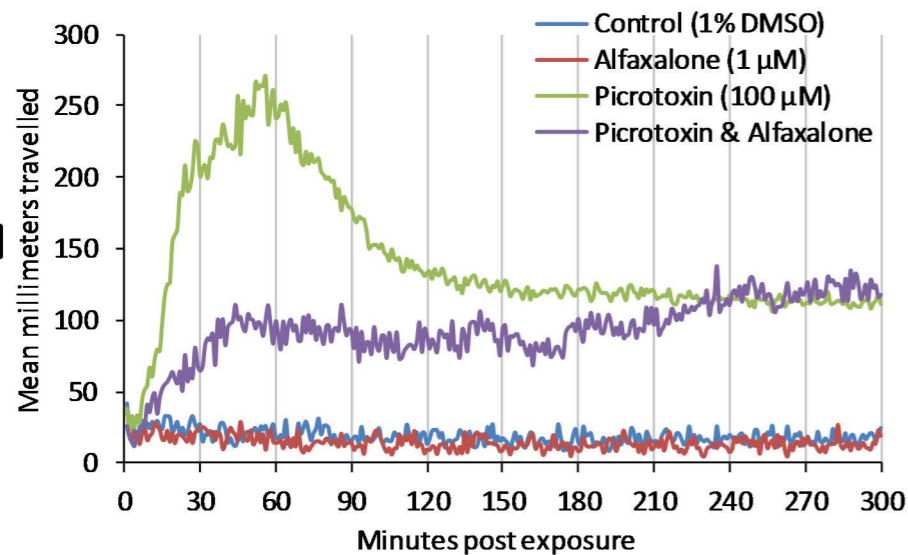
Picrotoxin  
(S)-Equol  
Kaempferol

**2 GABAergics:**

Alfaxalone  
Chlormethiazole

# CHEMICAL:

# Picrotoxin & Alfaxalone



## Normalized percent activity

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
Control (1% DMSO)	100 ± 73	100 ± 79	100 ± 59	100 ± 58	100 ± 62	100 ± 71	100 ± 68	100 ± 57	100 ± 56	100 ± 64	32
Alfaxalone (1 μM)	78 ± 66	93 ± 72	71 ± 58	76 ± 63	73 ± 59	78 ± 78	81 ± 72	70 ± 54	80 ± 73	78 ± 70	30
Picrotoxin (100 μM)	435 ± 131	165 ± 306	1048 ± 254	805 ± 267	710 ± 197	768 ± 124	731 ± 111	662 ± 109	649 ± 125	654 ± 138	32
Picrotoxin & Alfaxalone	177 ± 87	458 ± 194	463 ± 170	453 ± 162	496 ± 232	538 ± 257	583 ± 313	616 ± 247	673 ± 295	708 ± 315	31

## Mean ± standard deviation

## Normalized percent activity

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control (1% DMSO)	74-126	72-128	79-121	80-120	78-122	75-125	76-124	80-120	80-120	78-122
Alfaxalone (1 μM)	54-102	66-119	50-93	53-99	52-95	49-106	55-108	50-90	54-107	53-104
Picrotoxin (100 μM)	389-481	1047-1263	958-1138	711-900	641-780	724-812	692-771	624-701	605-693	605-702
Picrotoxin & Alfaxalone	145-208	389-528	402-524	395-512	413-580	446-630	471-696	527-705	566-779	595-821

## 95% confidence interval

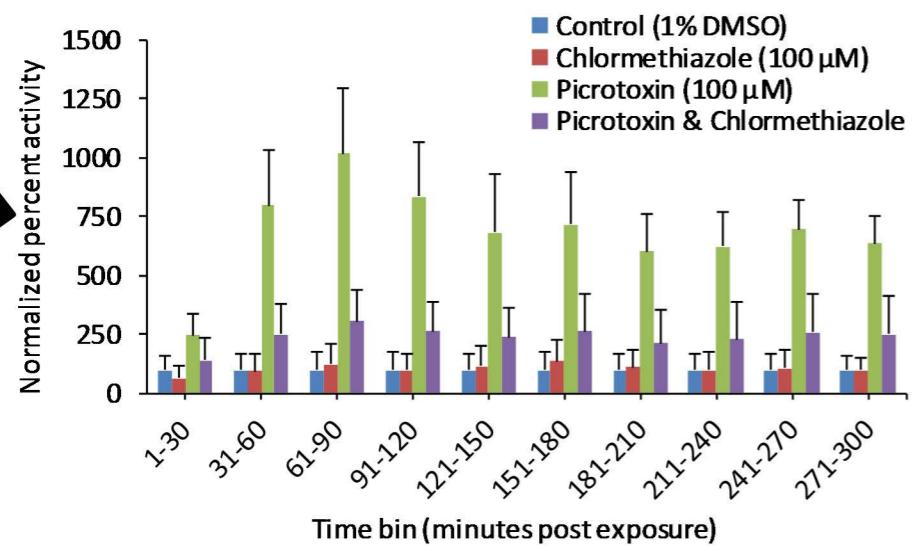
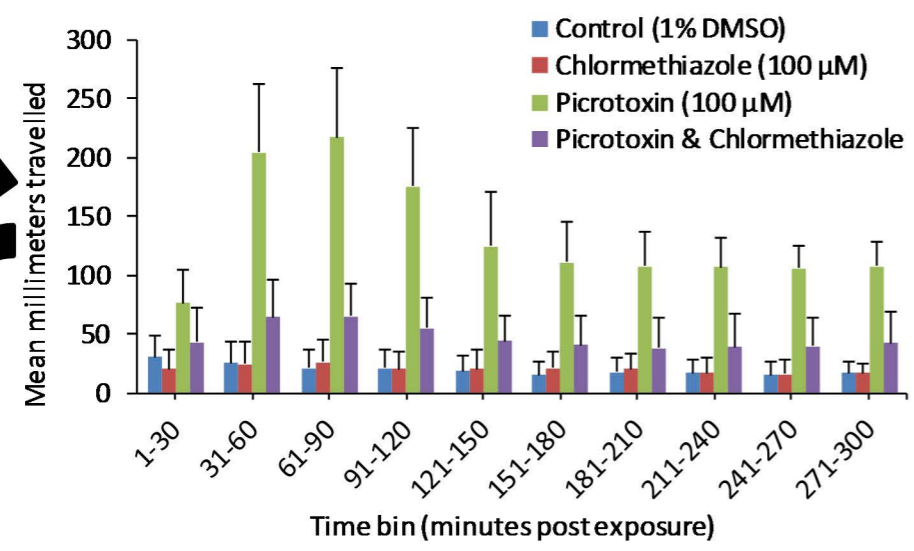
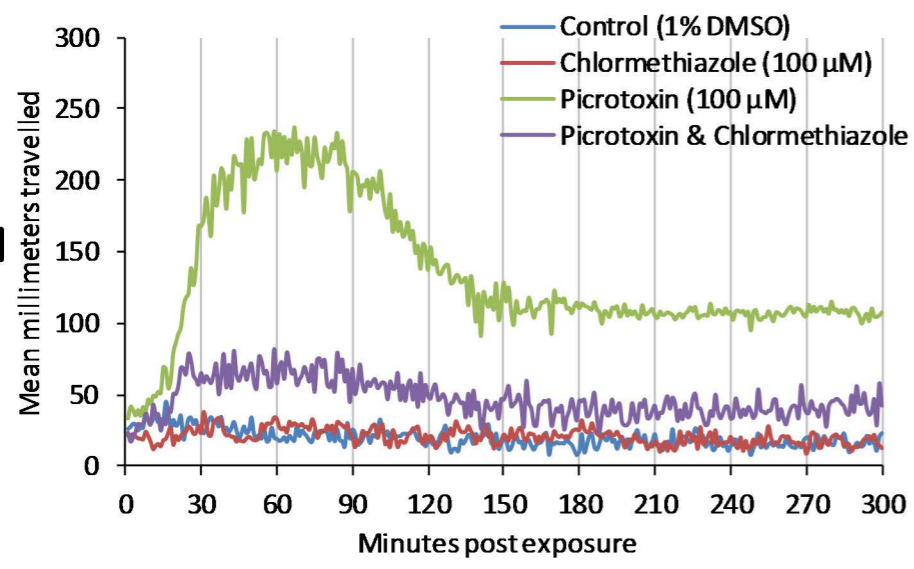
## p-values

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control vs. Alfaxalone	0.102	0.947	0.049	0.076	0.072	0.158	0.397	0.051	0.275	0.242
Control vs. Picrotoxin	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Control vs. Picrotoxin & Alfaxalone	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Alfaxalone vs. Picrotoxin	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Alfaxalone vs. Picrotoxin & Alfaxalone	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Picrotoxin vs. Picrotoxin & Alfaxalone	0.001	0.001	0.001	0.001	0.001	0.001	0.020	0.583	0.987	0.998

## Two-way repeated measures ANOVA, Tukey's post-hoc, p ≤ 0.05

# CHEMICAL: Picrotoxin & Chlormethiazole



## Normalized percent activity

Treatment	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
Control (1% DMSO)	100 ± 59	100 ± 72	100 ± 77	100 ± 76	100 ± 72	100 ± 74	100 ± 72	100 ± 67	100 ± 70	100 ± 62	31
Chlormethiazole (100 μM)	66 ± 54	96 ± 74	124 ± 86	98 ± 70	113 ± 85	137 ± 95	112 ± 74	98 ± 76	107 ± 81	98 ± 54	30
Picrotoxin (100 μM)	247 ± 94	799 ± 231	1016 ± 278	835 ± 233	682 ± 247	718 ± 221	603 ± 158	623 ± 144	694 ± 128	635 ± 121	31
Picrotoxin & Chlormethiazole	142 ± 95	251 ± 126	305 ± 131	262 ± 123	239 ± 122	264 ± 156	213 ± 145	229 ± 161	259 ± 160	249 ± 164	29

Mean ± standard deviation

## Normalized percent activity

Treatment	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control (1% DMSO)	79-121	74-126	72-128	73-127	74-126	73-127	74-126	76-124	75-125	78-122
Chlormethiazole (100 μM)	46-86	69-123	93-155	72-123	82-144	102-171	85-139	71-126	78-137	79-118
Picrotoxin (100 μM)	214-281	716-882	916-1116	751-918	593-770	638-797	546-660	571-674	648-740	591-678
Picrotoxin & Chlormethiazole	107-177	205-298	256-354	217-308	193-284	206-322	159-267	169-289	200-319	188-310

95% confidence interval

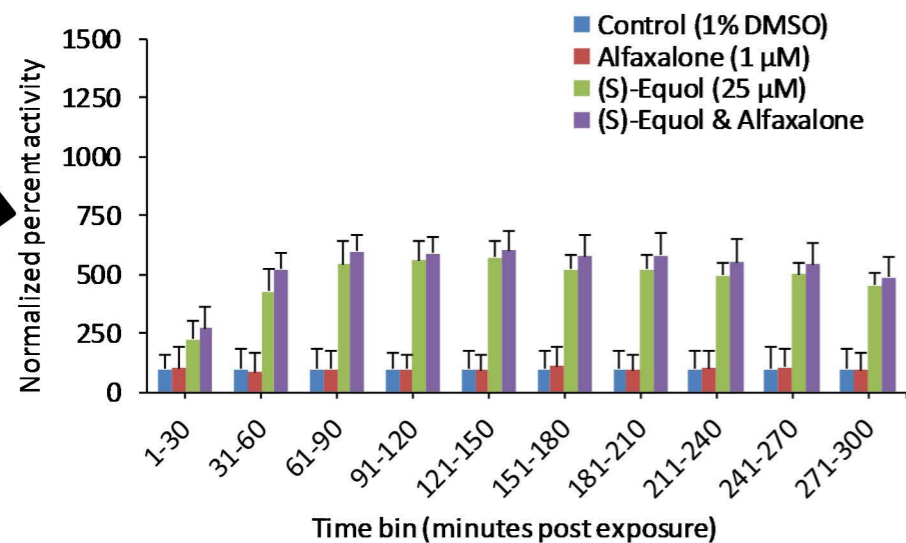
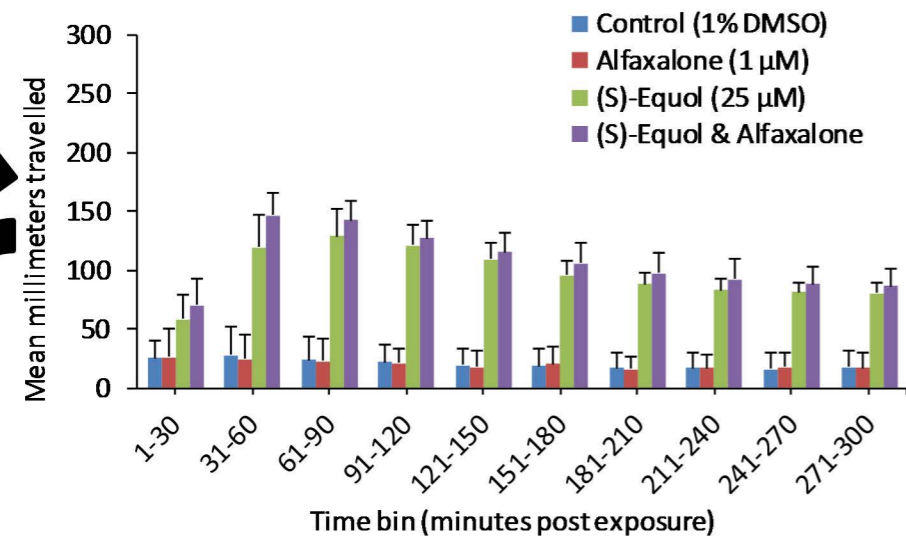
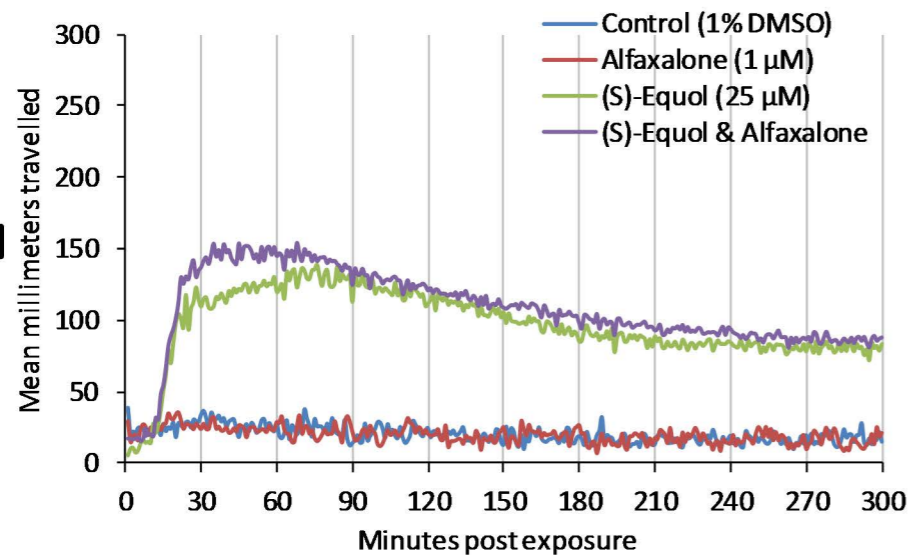
## p-values

Treatment	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control vs. Chlormethiazole	0.015	0.593	0.602	0.997	0.990	0.281	0.966	0.940	1.000	0.998
Control vs. Picrotoxin	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Control vs. Picrotoxin & Chlormethiazole	0.451	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Chlormethiazole vs. Picrotoxin	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Chlormethiazole vs. Picrotoxin & Chlormethiazole	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Picrotoxin vs. Picrotoxin & Chlormethiazole	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL:

# (S)-Equlol & Alfaxalone



## Normalized percent activity

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
Control (1% DMSO)	100 ± 59	100 ± 84	100 ± 81	100 ± 71	100 ± 73	100 ± 80	100 ± 80	100 ± 80	100 ± 90	100 ± 83	30
Alfaxalone (1 μM)	101 ± 93	88 ± 77	97 ± 77	99 ± 58	94 ± 67	111 ± 80	94 ± 64	103 ± 70	107 ± 80	93 ± 75	29
(S)-Equlol (25 μM)	227 ± 78	427 ± 99	542 ± 99	559 ± 82	571 ± 74	521 ± 66	522 ± 62	496 ± 52	500 ± 51	455 ± 50	31
(S)-Equlol & Alfaxalone	273 ± 86	522 ± 70	597 ± 72	588 ± 68	602 ± 83	578 ± 92	579 ± 100	552 ± 98	542 ± 94	487 ± 84	31

Mean ± standard deviation

## Normalized percent activity

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control (1% DMSO)	78-122	69-131	70-130	74-126	73-127	71-129	71-129	71-129	67-133	70-130
Alfaxalone (1 μM)	66-135	59-116	68-125	78-121	69-119	81-141	70-118	77-129	77-137	65-121
(S)-Equlol (25 μM)	199-255	391-463	507-578	529-588	544-597	498-545	500-545	477-514	482-519	437-473
(S)-Equlol & Alfaxalone	242-304	497-547	571-623	563-613	572-631	545-611	544-615	517-587	508-576	457-517

95% confidence interval

## p-values

### Time bin (minutes post exposure)

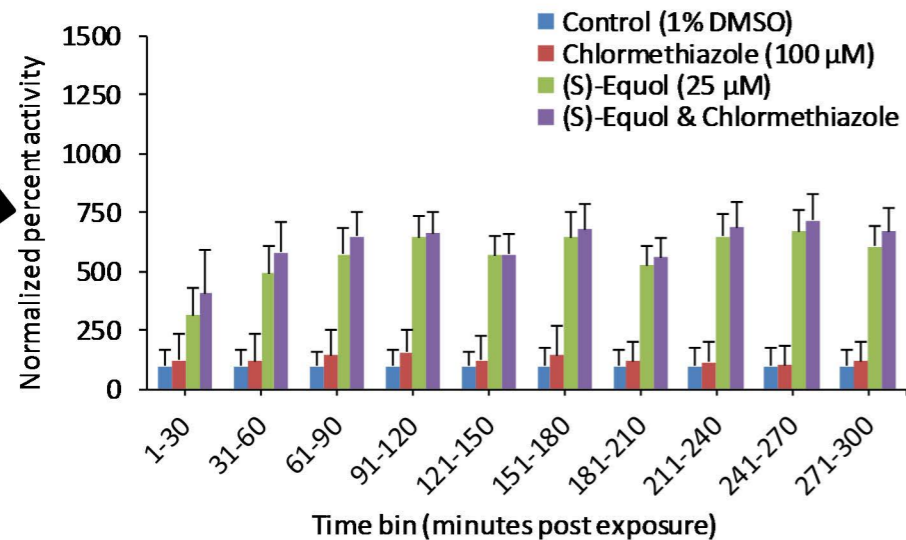
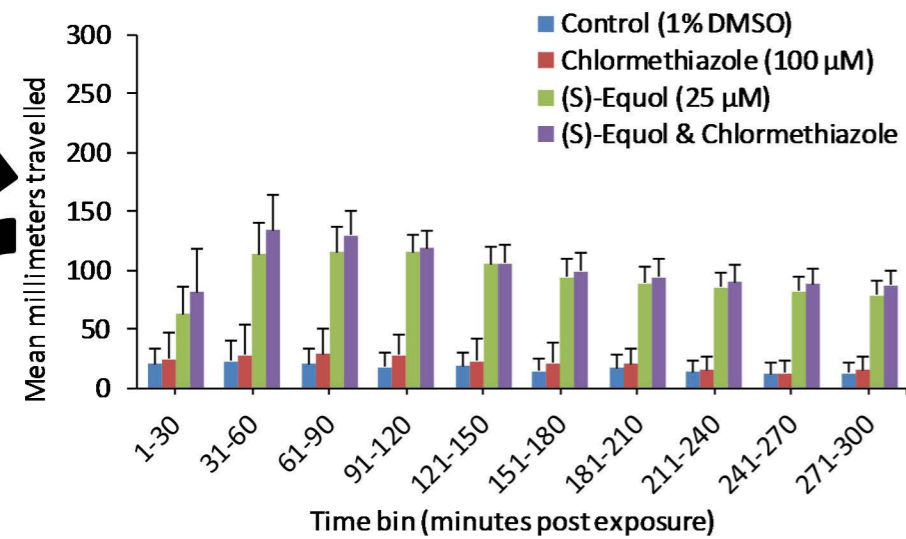
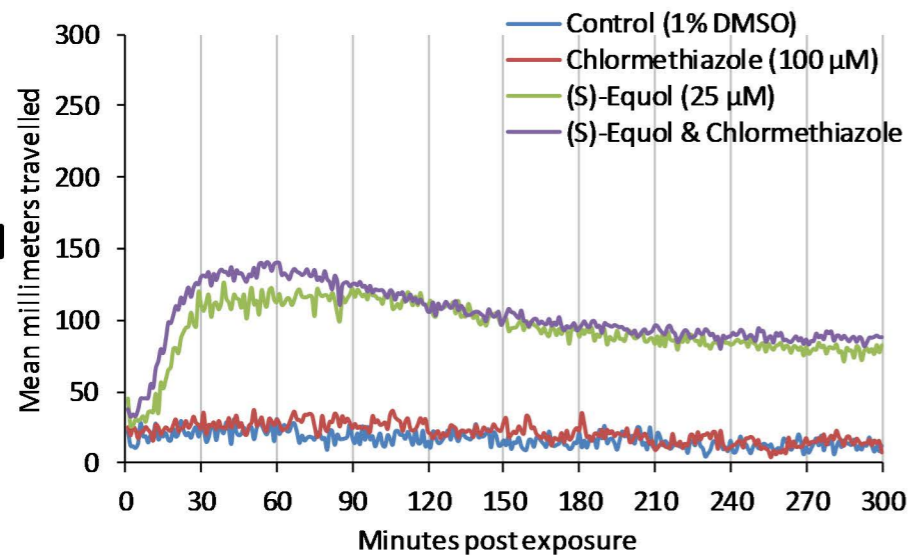
Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control vs. Alfaxalone	0.598	0.570	0.962	0.999	0.974	0.899	0.999	0.998	0.838	0.975
Control vs. (S)-Equlol	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Control vs. (S)-Equlol & Alfaxalone	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Alfaxalone vs. (S)-Equlol	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Alfaxalone vs. (S)-Equlol & Alfaxalone	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
(S)-Equlol vs. (S)-Equlol & Alfaxalone	0.188	0.009	0.429	0.867	0.893	0.546	0.601	0.593	0.797	0.861

Two-way repeated measures ANOVA, Tukey's post-hoc, p ≤ 0.05



# CHEMICAL:

# (S)-Equl & Chlormethiazole



## Normalized percent activity

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
Control (1% DMSO)	100 ± 67	100 ± 72	100 ± 63	100 ± 66	100 ± 63	100 ± 74	100 ± 67	100 ± 76	100 ± 73	100 ± 71	27
Chlormethiazole (100 μM)	123 ± 113	120 ± 113	145 ± 104	156 ± 99	122 ± 103	147 ± 122	118 ± 85	117 ± 87	101 ± 83	120 ± 83	29
(S)-Equl (25 μM)	313 ± 120	491 ± 118	574 ± 111	644 ± 87	567 ± 81	645 ± 111	527 ± 85	649 ± 95	669 ± 96	606 ± 89	31
(S)-Equl & Chlormethiazole	408 ± 180	580 ± 129	648 ± 102	664 ± 86	574 ± 87	680 ± 107	559 ± 88	685 ± 108	718 ± 107	669 ± 98	31

Mean ± standard deviation

## Normalized percent activity

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control (1% DMSO)	74-126	72-128	76-124	75-125	76-124	71-129	74-126	71-129	72-128	73-127
Chlormethiazole (100 μM)	81-165	78-162	107-184	119-193	84-161	101-192	86-150	85-150	70-131	89-150
(S)-Equl (25 μM)	270-356	449-533	535-614	613-676	538-596	606-685	497-557	615-683	634-703	574-638
(S)-Equl & Chlormethiazole	343-473	533-626	612-685	633-695	543-605	642-719	527-590	646-724	680-757	634-704

95% confidence interval

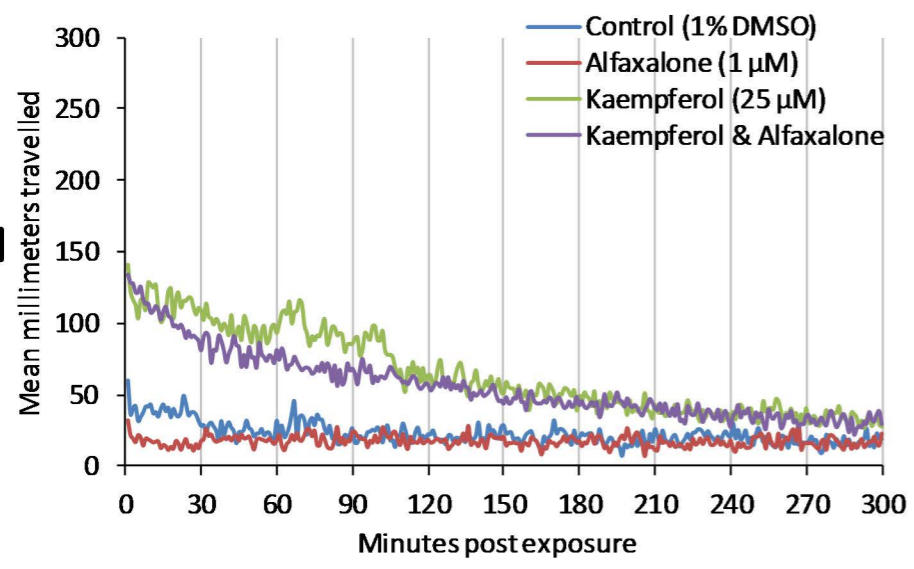
## p-values

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control vs. Chlormethiazole	0.996	0.958	0.133	0.034	0.944	0.227	0.848	0.852	0.999	0.829
Control vs. (S)-Equl	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Control vs. (S)-Equl & Chlormethiazole	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Chlormethiazole vs. (S)-Equl	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Chlormethiazole vs. (S)-Equl & Chlormethiazole	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
(S)-Equl vs. (S)-Equl & Chlormethiazole	0.026	0.058	0.244	0.974	0.998	0.892	0.863	0.903	0.798	0.586

Two-way repeated measures ANOVA, Tukey's post-hoc,  $p \leq 0.05$

# CHEMICAL: Kaempferol & Alfaxalone



**Normalized percent activity**

Treatment	Time bin (minutes post exposure)										N
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	
Control (1% DMSO)	100 ± 56	100 ± 69	100 ± 69	100 ± 75	100 ± 78	100 ± 72	100 ± 68	100 ± 61	100 ± 61	100 ± 57	32
Alfaxalone (1 μM)	41 ± 33	74 ± 57	69 ± 48	86 ± 55	82 ± 61	75 ± 59	90 ± 72	74 ± 69	89 ± 70	93 ± 71	32
Kaempferol (25 μM)	296 ± 119	383 ± 194	360 ± 208	351 ± 212	278 ± 140	243 ± 133	238 ± 139	178 ± 110	197 ± 117	193 ± 117	32
Kaempferol & Alfaxalone	271 ± 98	319 ± 132	256 ± 97	287 ± 120	250 ± 95	219 ± 83	237 ± 93	178 ± 84	181 ± 80	187 ± 87	32

Mean ± standard deviation

**Normalized percent activity**

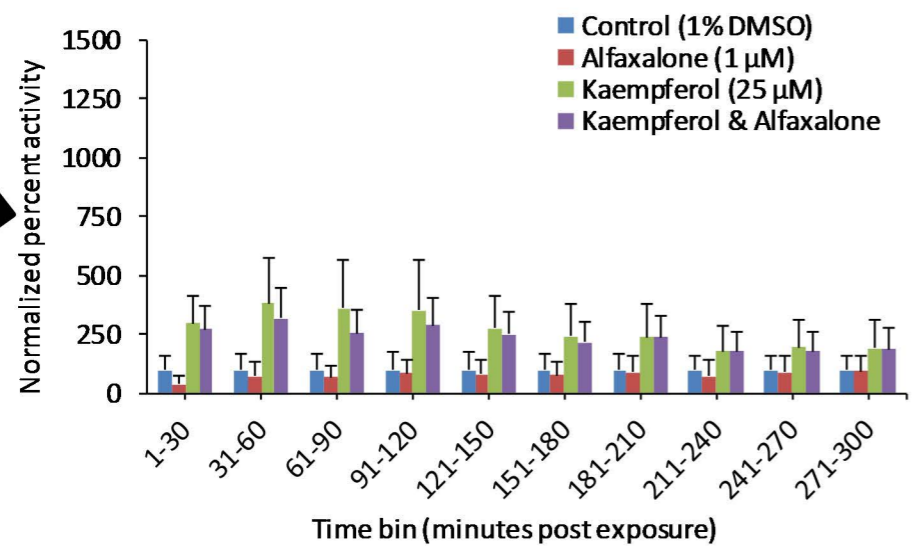
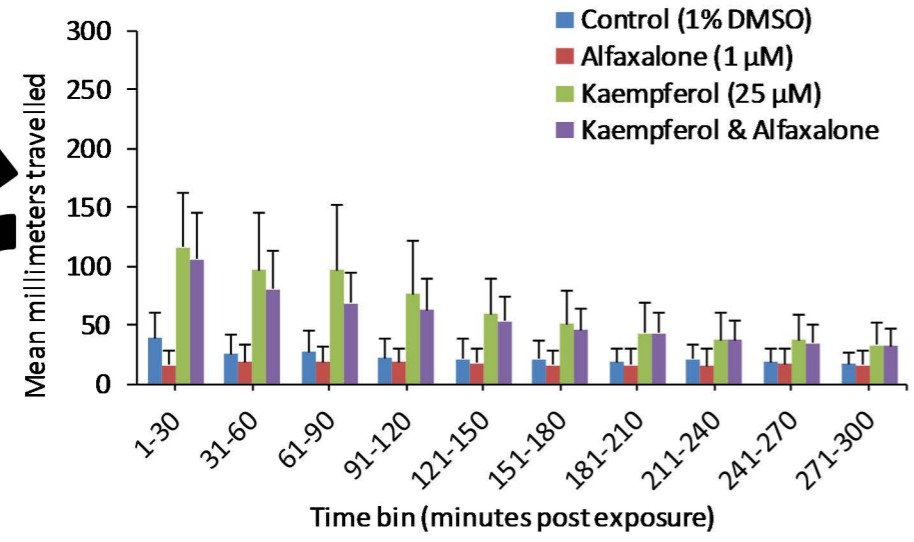
Treatment	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control (1% DMSO)	80-120	76-124	75-125	73-127	72-128	74-126	76-124	78-122	78-122	80-120
Alfaxalone (1 μM)	29-53	53-94	52-86	66-105	60-103	54-96	65-116	50-99	64-114	68-118
Kaempferol (25 μM)	254-338	314-451	286-433	276-426	229-328	196-290	189-287	139-217	155-238	151-234
Kaempferol & Alfaxalone	236-306	272-365	222-290	245-330	217-284	189-248	204-269	148-208	153-209	156-218

95% confidence interval

**p-values**

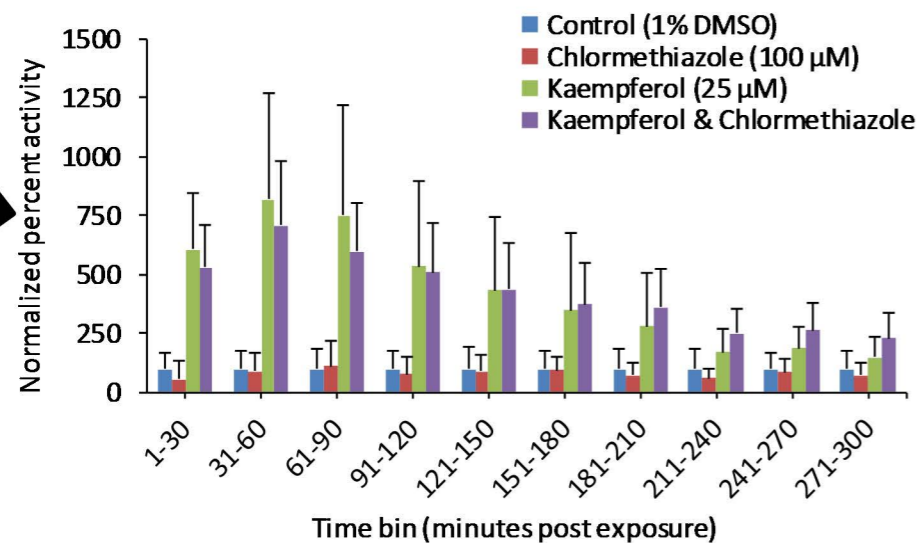
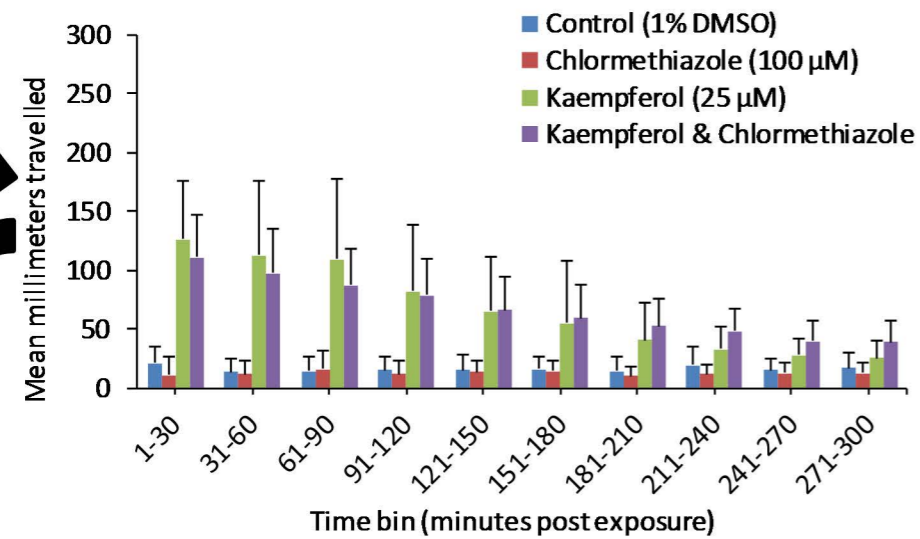
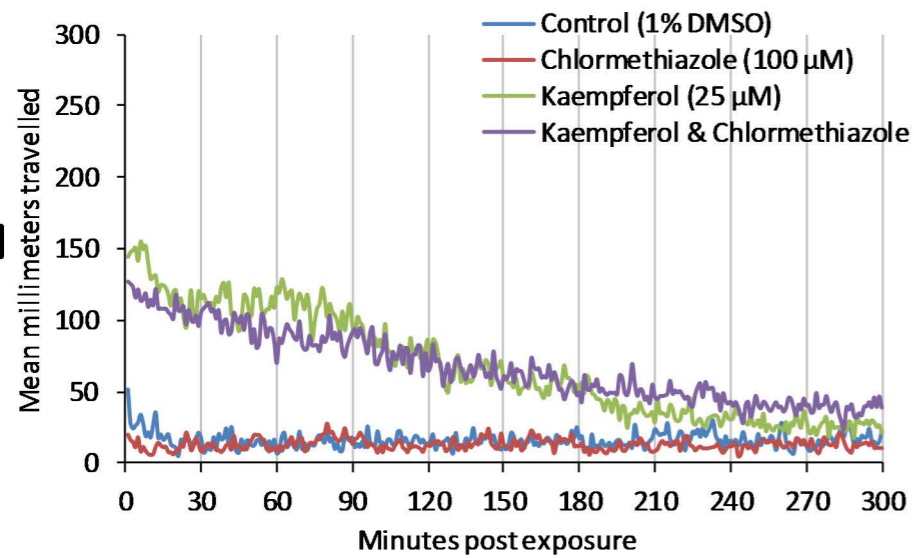
Treatment	Time bin (minutes post exposure)									
	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control vs. Alfaxalone	0.001	0.218	0.192	0.920	0.757	0.470	0.928	0.071	0.876	0.877
Control vs. Kaempferol	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.013	0.001	0.003
Control vs. Kaempferol & Alfaxalone	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001
Alfaxalone vs. Kaempferol	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Alfaxalone vs. Kaempferol & Alfaxalone	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Kaempferol vs. Kaempferol & Alfaxalone	0.903	0.660	0.197	0.743	0.980	0.997	0.882	0.942	1.000	0.998

Two-way repeated measures ANOVA, Tukey's post-hoc, p ≤ 0.05



# CHEMICAL:

# Kaempferol & Chlormethiazole



## Normalized percent activity

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	N
Control (1% DMSO)	100 ± 67	100 ± 77	100 ± 83	100 ± 78	100 ± 90	100 ± 73	100 ± 84	100 ± 86	100 ± 70	100 ± 76	28
Chlormethiazole (100 μM)	54 ± 78	89 ± 83	111 ± 110	78 ± 75	91 ± 68	92 ± 59	72 ± 57	62 ± 42	84 ± 59	74 ± 55	30
Kaempferol (25 μM)	605 ± 239	816 ± 454	750 ± 469	534 ± 363	434 ± 309	346 ± 333	281 ± 225	171 ± 102	188 ± 94	150 ± 88	29
Kaempferol & Chlormethiazole	531 ± 179	707 ± 274	600 ± 207	511 ± 206	438 ± 193	375 ± 172	362 ± 164	251 ± 100	264 ± 114	228 ± 108	28

Mean ± standard deviation

## Normalized percent activity

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control (1% DMSO)	75-125	71-129	69-131	70-130	66-134	72-128	68-132	67-133	73-127	71-129
Chlormethiazole (100 μM)	26-83	59-119	70-151	51-106	66-116	71-114	51-93	47-77	62-105	53-94
Kaempferol (25 μM)	517-694	648-985	576-925	399-669	319-548	222-470	198-365	133-208	153-222	117-183
Kaempferol & Chlormethiazole	464-599	603-810	521-678	433-588	366-511	310-440	300-425	213-289	221-307	188-269

95% confidence interval

## p-values

### Time bin (minutes post exposure)

Treatment	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300
Control vs. Chlormethiazole	0.001	0.629	0.999	0.302	0.947	0.922	0.508	0.226	0.851	0.677
Control vs. Kaempferol	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.011	0.004	0.076
Control vs. Kaempferol & Chlormethiazole	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Chlormethiazole vs. Kaempferol	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002
Chlormethiazole vs. Kaempferol & Chlormethiazole	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
Kaempferol vs. Kaempferol & Chlormethiazole	0.895	0.963	0.884	0.937	0.883	0.375	0.130	0.023	0.113	0.030

Two-way repeated measures ANOVA, Tukey's post-hoc, p ≤ 0.05