DEBtox Research

Ring test results for BYOM

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1 Background

Full details of the GUTS ring test are provided in the e-book [1]. Here, I will only present the results for the BYOM platform, including both likelihood-based and Bayesian intervals. The data sets and the exposure profiles are provided in an Excel file that can be downloaded from http://www.debtox.info/book_guts.html.

Likelihood-based intervals. Profile likelihood for individual parameters (automated procedure with variable step size), 10 sub-optimisations used at each evaluation point when test phase indicated that was needed. Likelihood-region for joint intervals (used for forward predictions), 10 sub-optimisations used when test phase indicated that was needed. Sampling (LHS) continued in bursts until at least 5000 samples from the joint interval were found. For forward predictions, the min-max of all the curves from these 5000 samples is used for the CI on the predictions (only for data set C, SD with Focus scenario, 500 samples due to extreme calculation times).

Bayesian intervals. MCMC sampling using the Matlab slice sampler. 10000 samples kept, after 100 burn-in samples and thinning of 10-20 (keeping one in every 10-20 samples). Slice sampling was done on log scale (but priors were uniform on normal scale). Thinning and log-scale were needed to keep autocorrelation in the sample within reasonable bounds. For forward predictions, the 0.025 and 0.975 quantiles of all curves from the sample were used for the CIs. Only for data set C, SD with Focus scenario, 1000 samples due to extreme calculation times.

Time-varying exposure. Exposure scenario is interpolated using cubic hermite spline.

2 Data set A

Analytical solution used for fitting.

Table 1: Parameters for the fits on data sets A (separate data sets for SD and IT), with the predictions for the 4-day and 30-day LC50. Note that β is simply calculated from the fitted F_s; both are measures for the spread of the threshold distribution.

		GUTS-RED-SD	minloglik = 96.45
Param.	Optimum	Likelihood CI	Bayes CI
k_d	0.7118	0.4983 - 0.9798	0.4687 - 0.9656
m_w	2.885	2.292 - 3.355	2.174 - 3.296
h_b	0.008004	0.001337 - 0.02524	0.00113 - 0.02272
b_w	0.6187	0.4136 - 1.090	0.3956 - 1.006
4-d LC50	3.948	3.376 - 4.393	3.558 - 4.228
30-d LC50	2.934	1.947 - 3.555	2.238 - 3.329
		GUTS-RED-IT	minloglik = 116.02
Param.	Optimum	Likelihood CI	Bayes CI
k_d	0.7933	0.5588 - 1.106	0.5243 - 1.079
m_w	5.418	4.482 - 6.407	4.335 - 6.377
h_b	0.02624	0.01026 - 0.05163	0.009017 - 0.05006
F_s	2.025	1.645 - 2.687	1.688 - 2.947
β	5.192	3.706 - 7.360	3.390 - 6.998
4-d LC50	5.655	4.571 - 7.061	4.831 - 6.511
30-d LC50	5.418	3.947 - 6.982	4.346 - 6.356

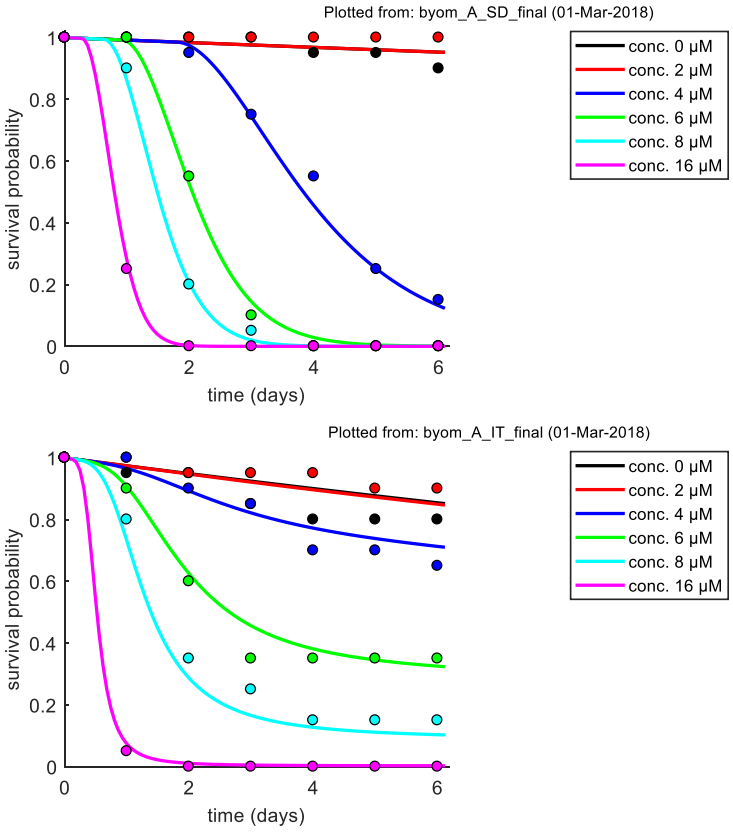

Figure 1: Fits for data set A SD (top) and IT (bottom).

3 Data set B

3.1 Constant exposure

Analytical solution used for fitting.

Table 2: Parameters for the fits on data set B (same data set for SD and IT), with the predictions for the 4-day and 30-day LC50. Note that β is simply calculated from the fitted F_s; both are measures for the spread of the threshold distribution.

		GUTS-RED-SD	minloglik = 123.83
Param.	Optimum	Likelihood CI	Bayes CI
k_d	2.160	1.598 - 3.333	1.589 - 3.71
m_w	17.06	15.86 - 17.74	15.51 - 18.95
h_b	0.02755	0.01333 - 0.04952	0.01296 - 0.05105
b_w	0.1318	0.08637 - 0.1957	0.07733 - 0.1900
4-d LC50	19.15	17.60 - 21.91	18.10 - 20.78
30-d LC50	17.25	15.10 - 20.54	15.78 - 19.10
		GUTS-RED-IT	minloglik = 127.75
Param.	Optimum	Likelihood CI	Bayes CI
k_d	0.7500	0.5564 - 0.9770	0.5109 - 0.9538
m_w	18.06	15.45 - 20.60	14.82 - 20.43
h_b	0.01858	0.004973 - 0.04141	0.002415 - 0.03953
F_s	1.683	1.475 - 2.024	1.506 - 2.184
β	7.037	5.196 - 9.426	4.690 - 8.947
4-d LC50	19.00	16.23 - 22.35	16.84 - 20.94
30-d LC50	18.06	13.97 - 21.98	14.86 - 20.38

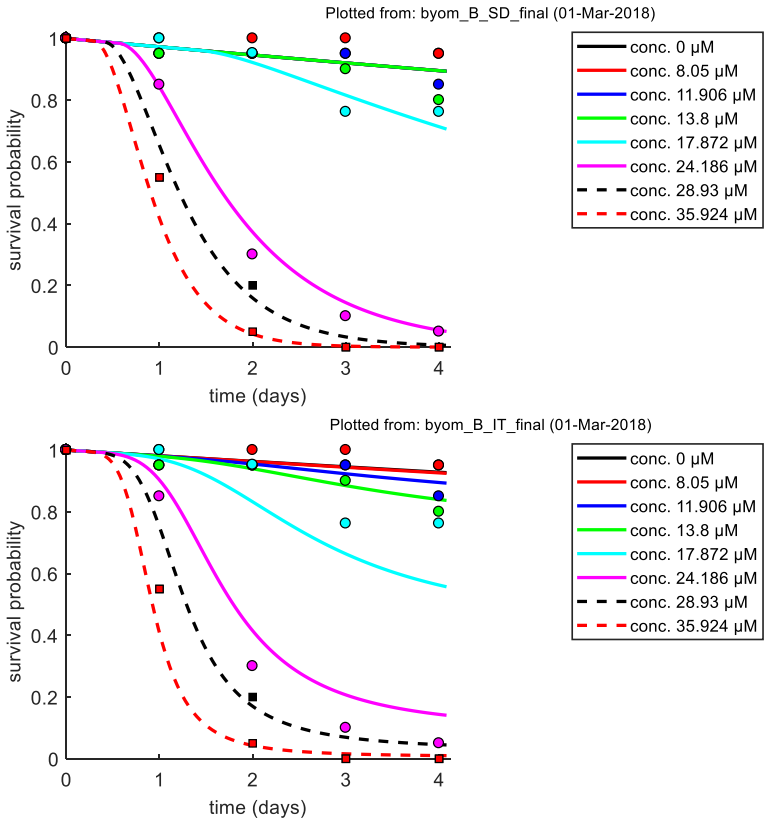

Figure 2: Fits for data set B, constant exposure, SD (top) and IT (bottom).

3.2 Time-varying exposure

ODE solver (`ode113`) used for fitting. Bayesian analysis not shown as it got stuck.

Table 3: Parameters for the fits on data set B (same data set for SD and IT), with the predictions for the 4-day and 30-day LC50. Note that β is simply calculated from the fitted F_s; both are measures for the spread of the threshold distribution.

		GUTS-RED-SD	minloglik = 328.23
Param.	Optimum	Likelihood CI	Bayes CI
k_d	2.519	1.387 - 10	
m_w	23.00	18.66 - 26.70	
h_b	0.02411	0.01761 - 0.03189	
b_w	0.2781	0.04808 - 1.025	
4-d LC50	24.06	18.64 - 29.32	
30-d LC50	23.09	7.274 - 27.68	
		GUTS-RED-IT	minloglik = 330.54
Param.	Optimum	Likelihood CI	Bayes CI
k_d	0.8523	0.4640 - 10.00	
m_w	17.59	15.30 - 32.87	
h_b	0.02629	0.01979 - 0.03409	
F_s	1.260	1.089 - 5.553	
β	15.85	2.137 - 42.97	
4-d LC50	18.19	18.39 - 100.4	
30-d LC50	17.59	10.61 - 100.3	

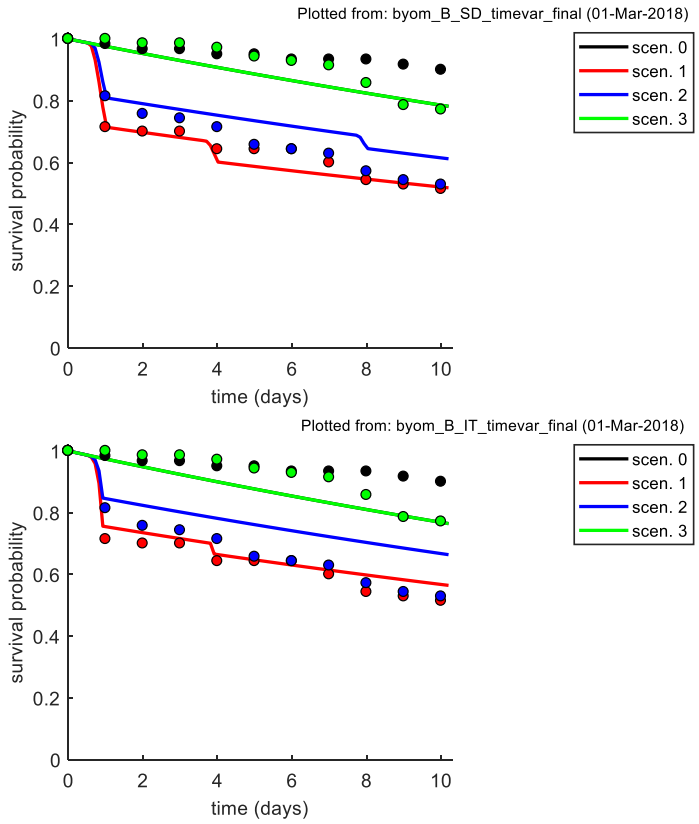

Figure 3: Fits for data set B, time-varying exposure, SD (top) and IT (bottom).

3.3 Constant and time-varying exposure, simultaneously

ODE solver (`ode113`) used for fitting. Bayesian analysis not shown as it got stuck.

Table 4: Parameters for the fits on data set B (same data set for SD and IT), with the predictions for the 4-day and 30-day LC50. Note that β is simply calculated from the fitted F_s; both are measures for the spread of the threshold distribution.

		GUTS-RED-SD	minloglik = 460.33
Param.	Optimum	Likelihood CI	Bayes CI
k_d	1.651	1.371 - 2.082	
m_w	17.06	15.92 - 19.98	
h_b	0.02360	0.01768 - 0.03052	
b_w	0.1352	0.08464 - 0.2175	
4-d LC50	19.46	18.04 - 22.96	
30-d LC50	17.25	15.35 - 21.73	
		GUTS-RED-IT	minloglik = 458.843
Param.	Optimum	Likelihood CI	Bayes CI
k_d	0.7915	0.6489 - 0.8945	
m_w	18.52	16.69 - 20.04	
h_b	0.02554	0.01938 - 0.03266	
F_s	1.650	1.483 - 1.933	
β	7.316	5.559 - 9.297	
4-d LC50	19.33	17.28 - 21.59	
30-d LC50	18.52	15.77 - 21.19	

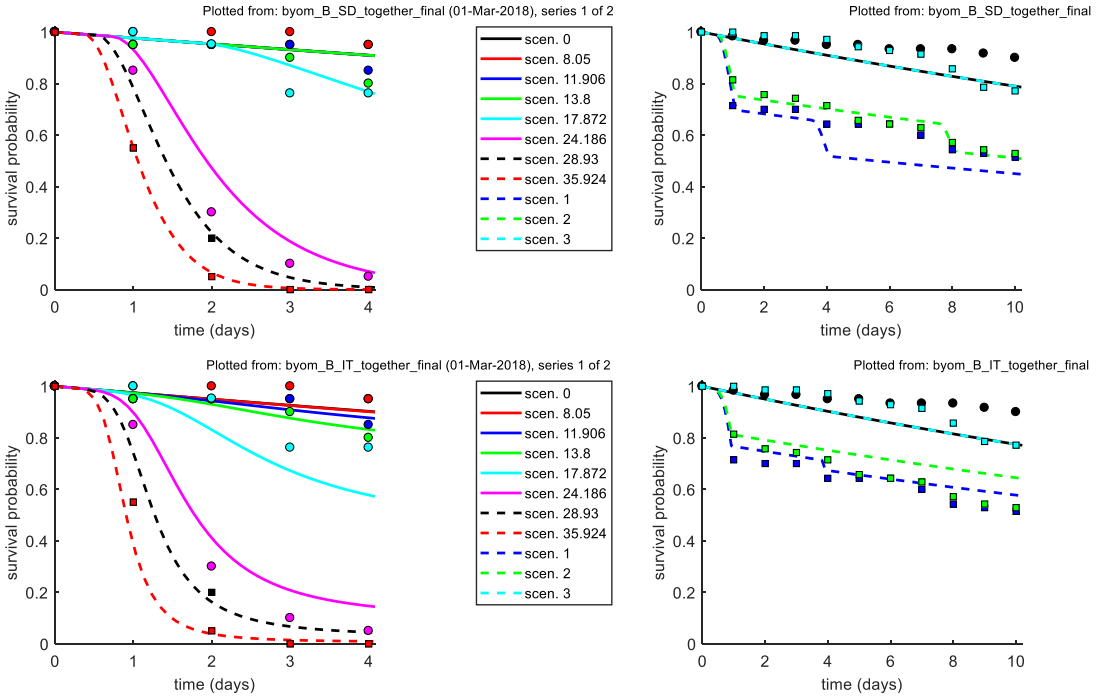

Figure 4: Fits for data set B, time-varying exposure, SD (top) and IT (bottom).

4 Data set C

Analytical solution used for fitting. For two exposure scenarios (Focus and monitor), the LP10 is calculated: the factor by which the entire profile needs to be multiplied to reach 10% mortality at the end of the profile. For the predictions of the LP10, the dominant rate constant (k_d) max maximised at 10 d^{-1}, and for SD in the Focus scenario, a smaller number of samples was used due to the long calculation times (500 for the likelihood-based analysis, and 1000 for the Bayesian). The background mortality (h_b) was fixed to zero for this data set.

Table 5: Parameters for the fits on data sets C (same data set for SD and IT), with the predictions for the 4-day and 30-day LC50. Note that β is simply calculated from the fitted F_s; both are measures for the spread of the threshold distribution.

		GUTS-RED-SD	minloglik = 63.13
Param.	Optimum	Likelihood CI	Bayes CI
k_d	100	7.675 - 100	6.875 - 95.72
m_w	6.158	4.9 - 6.617	4.511 - 6.56
h_b	0	n.e.	n.e.)
b_w	0.08244	0.0519 - 0.1204	0.04644 - 0.1154
4-d LC50	8.273	7.016 - 9.693	7.357 - 9.191
30-d LC50	6.439	4.694 - 6.972	4.952 - 6.786
LP10 Focus	4681	3541 - 4979	3564 - 4941
LP10 Monitor	43215	34876 - 46412	35491 - 45690
		GUTS-RED-IT	minloglik = 61.29
Param.	Optimum	Likelihood CI	Bayes CI
k_d	1.262	0.9073 - 1.682	0.8655 - 1.671
m_w	9.336	8.091 - 10.73	7.988 - 10.87
h_b	0	n.e.	n.e.
F_s	2.252	1.8 - 3.234	1.854 - 3.684
β	4.513	3.121 - 6.233	2.809 -5.934
4-d LC50	9.396	7.715 - 11.45	8.161 - 10.90
30-d LC50	9.336	7.555 - 11.41	7.992 - 10.83
LP10 Focus	4828	3496 - 5777	3558 - 5606
LP10 Monitor	38193	28339 - 45108	29037 - 44033

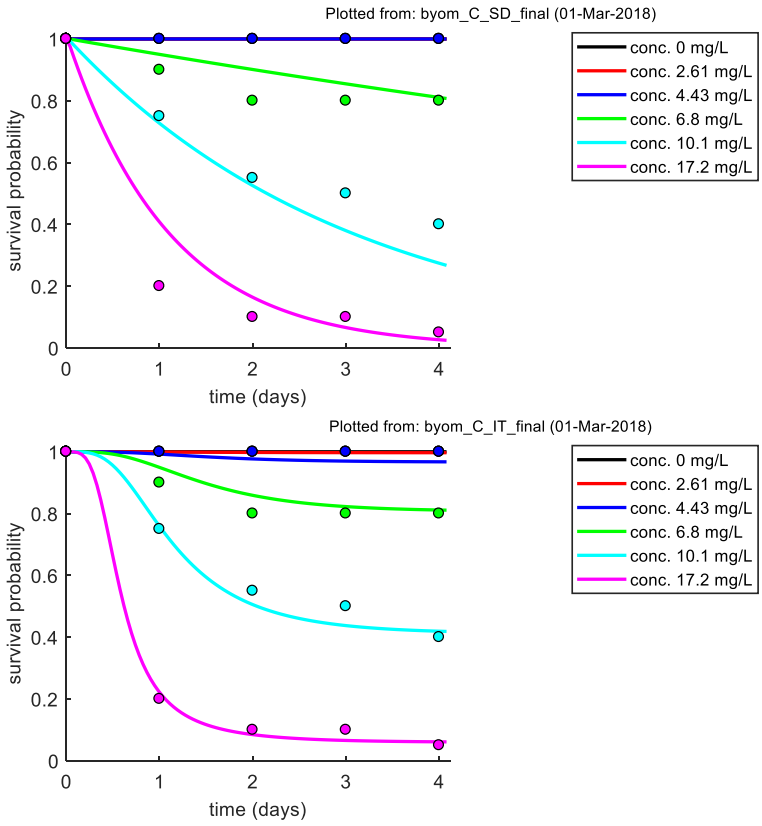

Figure 5: Fits for data set C SD (top) and IT (bottom).

References

[1] T. Jager and R. Ashauer. *Modelling survival under chemical stress. A comprehensive guide to the GUTS framework*. Toxicodynamics Ltd., York, UK. Available from Leanpub, https://leanpub.com/guts_book, Version 1.0, 18 January 2018, 2018.