MOSAIC$_{\text{bioacc}}$ REPORT

2021-05-12

This report is provided by the MOSAIC$_{\text{bioacc}}$ application available here: https://mosaic.univ-lyon1.fr/bioacc

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MOSAIC$_{\text{bioacc}}$ uses the JAGS (version 4.3.0) and R (version 4.0.2) software, and in particular packages RJags (version 4.10), jagsUI (version 1.5.1) and Shiny (version 1.6.0).

The MOSAIC$_{\text{bioacc}}$ application is a turn-key web tool providing bioaccumulation factors (BCF/BSAF/BMF) from a toxicokinetic (TK) model fitted to accumulation-depuration data. It is designed to fulfil the requirements of regulators when examining applications for market authorization of active substances.

Data summary

File used: Gammarus_epoxiconazole_1d_Rosch2016.txt

Exposure: 100 $\mu g.mL^{-1}$

Accumulation phase duration: 1 days

Number of replicates: 3

Times: 0, 0.24, 0.4, 0.75, 1, 1.05, 1.09, 1.18, 1.3, 1.46, 1.75, 2.08, 2.71, 3.1, 3.95, 5

Exposure routes: water

Elimination routes: excretion biotransformation

Bayesian inference

Three MCMC chains were used to estimate model parameters.

Number of iterations: 52444

Thin: 14

TK Model

The TK model used for these calculations was:

$$\frac{dC_p(t)}{dt} = k_{uw} \times c_w - (k_{ee} + k_{m1} + k_{m2} + k_{m3}) \times C_p(t) \quad for\ 0 \leq t \leq t_c$$

$$\frac{dC_p(t)}{dt} = -(k_{ee} + k_{m1} + k_{m2} + k_{m3}) \times C_p(t) \quad for\ t > t_c$$

$$\frac{dC_{m1}(t)}{dt} = k_{m1} \times C_p(t) - k_{em1} \times C_{m1}(t)$$

$$\frac{dC_{m2}(t)}{dt} = k_{m2} \times C_p(t) - k_{em2} \times C_{m2}(t)$$

$$\frac{dC_{m3}(t)}{dt} = k_{m3} \times C_p(t) - k_{em3} \times C_{m3}(t)$$

with:

t: time (expressed in days)

t_c: duration of the accumulation phase (expressed in days)

$C_p(t)$: internal concentration of the parent compound at time (expressed in $\mu g.g^{-1}$)

k_{ee}: elimination rates of excretion (expressed per days $^{-1}$)

c_w: exposure concentration of water route (expressed in $\mu g.mL^{-1}$)

k_{uw}: uptake rate of water exposure (expressed per days $^{-1}$)

$C_{m\ell}(t)$: internal concentration of metabolite ℓ (expressed in $\mu g.g^{-1}$)

ℓ: index of metabolites, $\ell = 1 \ldots L$ with L total number of metabolites

$k_{m\ell}$: metabolization rate of metabolite ℓ (expressed per days $^{-1}$)

$k_{em\ell}$: elimination rates of metabolite ℓ (expressed per days $^{-1}$)
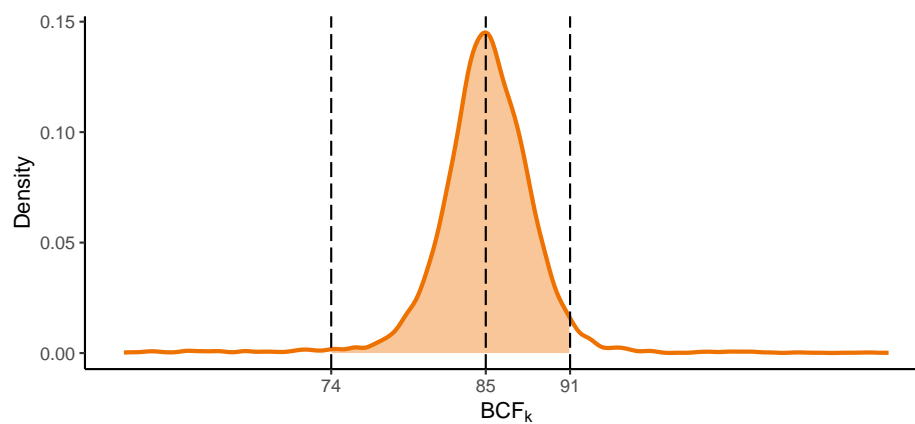
Bioaccumulation factor calculation

Calculations

$$BCF_k = \frac{k_{uw}}{k_{ee} + k_{m1} + k_{m2} + k_{m3}}$$

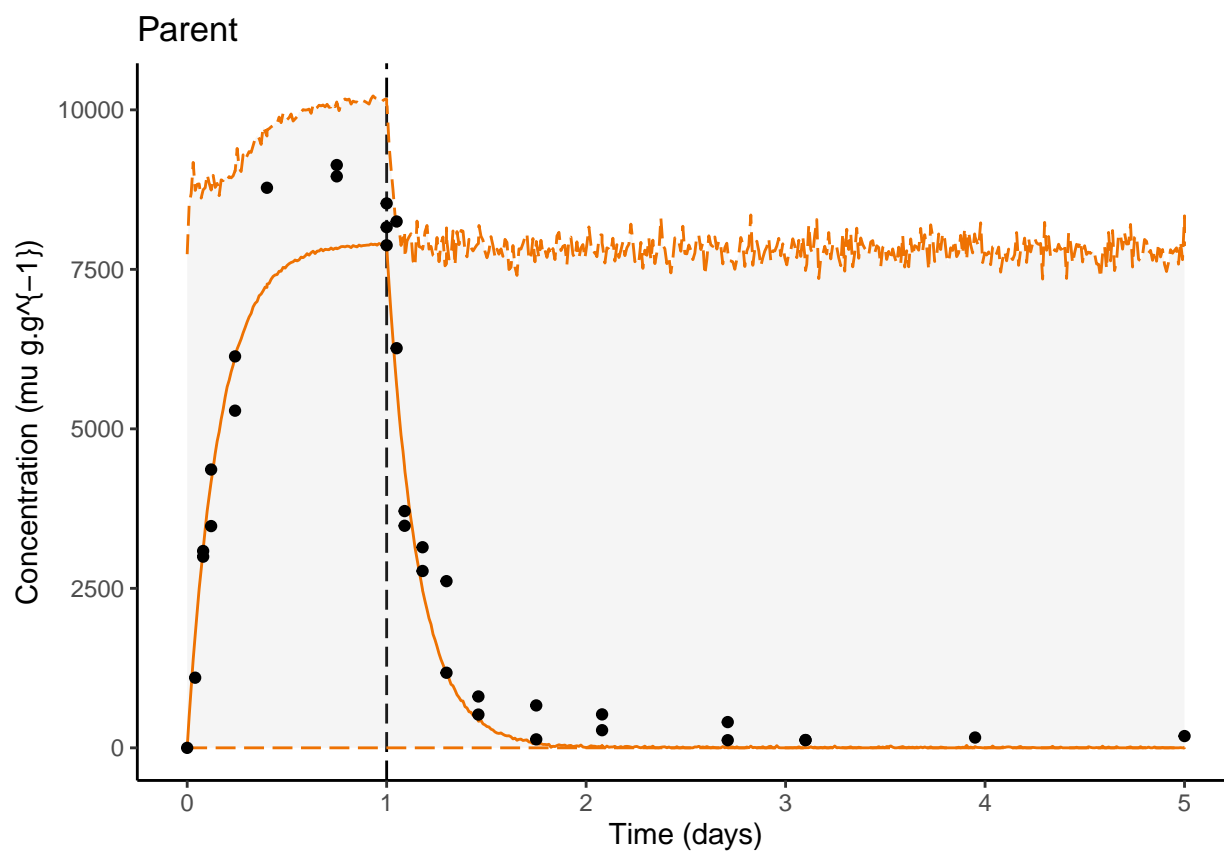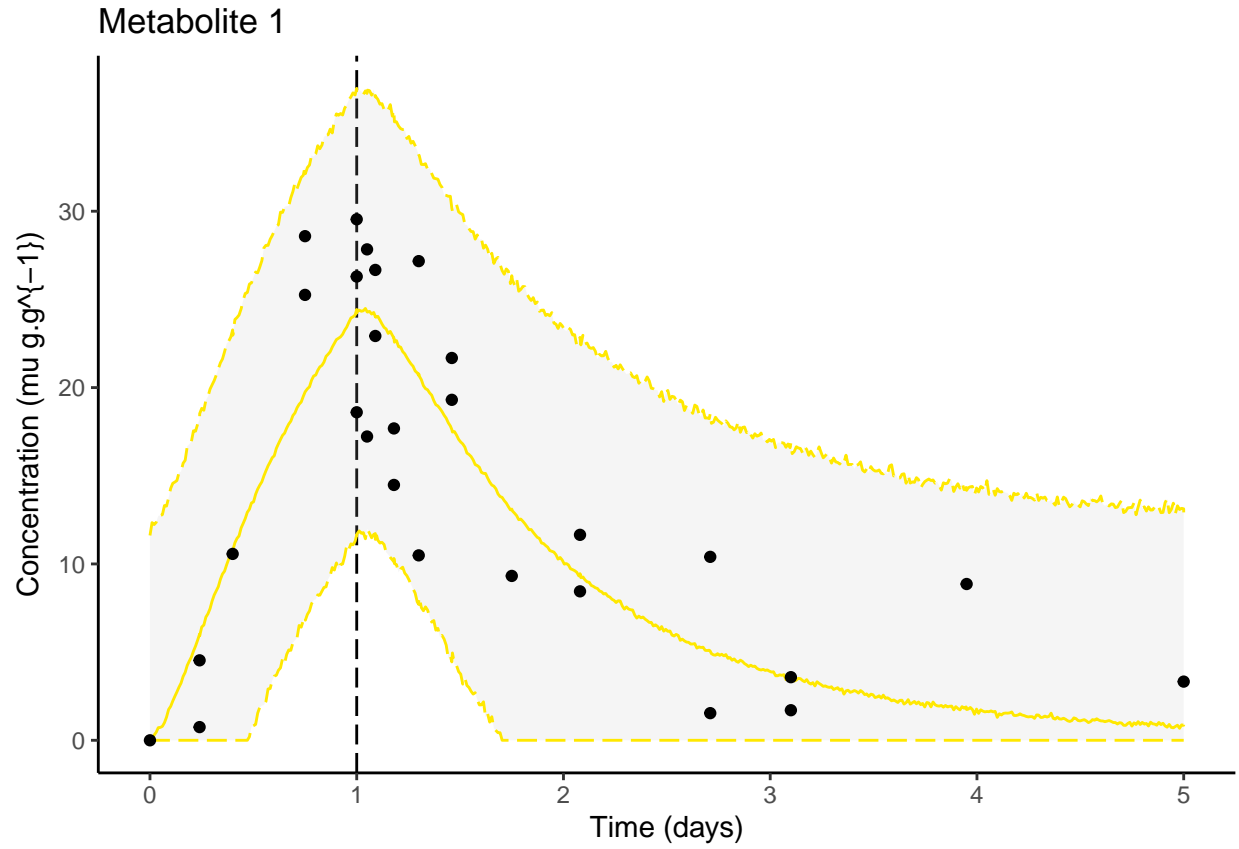$$BCF_{ss} = \frac{C_p(t_c)}{c_w}$$

Bioconcentration factor (BCF)

BCF$_{\mathbf{k}}$ plot
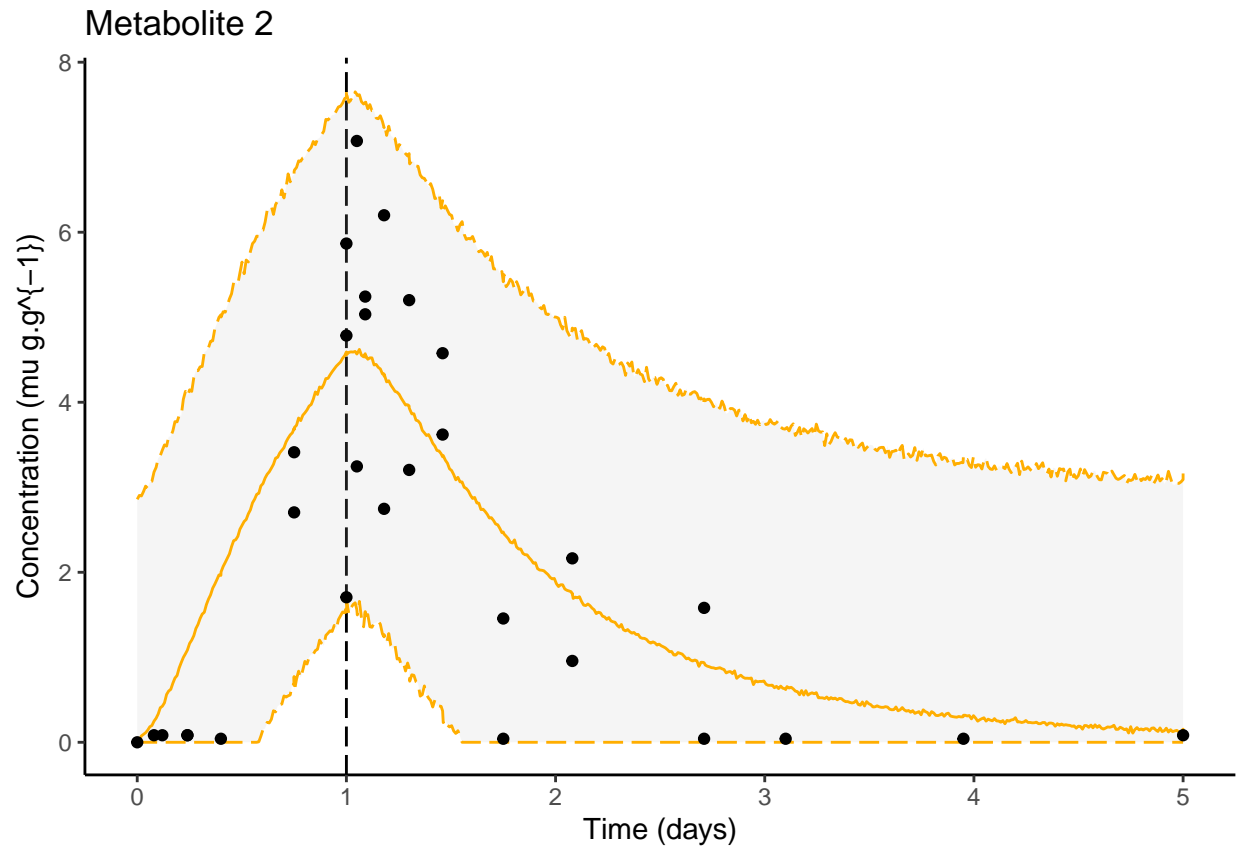

BCF summary

	2.5%	50%	97.5%	CV
BCFk	74	85	91	0.05

Fitting results

Fit plot

Parent

Metabolite 1

Metabolite 2

Metabolite 3
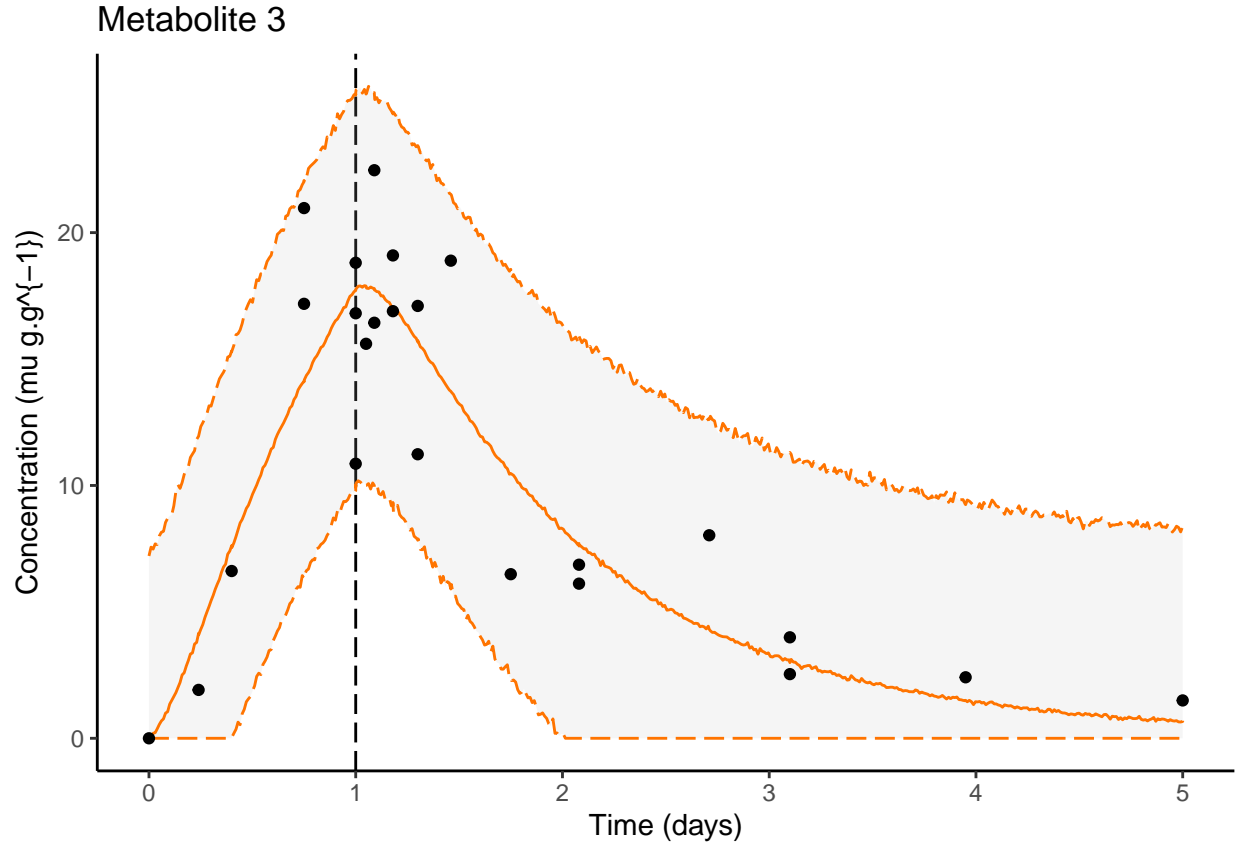
Quantiles of estimated parameters

	2.5%	50%	97.5%	
k_{uw}	0.6394	502.7	16130	d^{-1}
k_{ee}	7.644e-05	6.311	47530	d^{-1}
k_{m1}	0.003788	0.006596	12300	d^{-1}
k_{m2}	0.0007372	0.001206	2314	d^{-1}
k_{m3}	0.002936	0.004272	8811	d^{-1}
k_{em1}	0.4597	1.07	2.761	d^{-1}
k_{em2}	0.4617	1.104	2.31	d^{-1}
k_{em3}	0.4888	0.9603	1.877	d^{-1}
σ_p	561.2	839	6758	$\mu g.g^{-1}$
σ_{met1}	4.304	5.81	8.535	$\mu g.g^{-1}$
σ_{met2}	1.026	1.394	2.022	$\mu g.g^{-1}$
σ_{met3}	2.691	3.595	5.156	$\mu g.g^{-1}$

Goodness-of-fit criteria

Posterior Predictive Check

The PPC shows the observed values against their corresponding estimated predictions (black dots), along with their 95% credible interval (vertical segments). If the fit is correct, we expect to see 95% of the data within the intervals. Ideally observations and predictions should coincide, so we would expect to see black dots along the first bisector $y = x$ (plain black line). The 95% credible intervals are colored in green if they overlap this line, in red otherwise.

Parent compound:

percentage of data in CI:

100% (22/22)

Metabolite1:

percentage of data in CI:

100% (22/22)

Metabolite2:

percentage of data in CI:

100% (22/22)

Metabolite3:

percentage of data in CI:

100% (22/22)
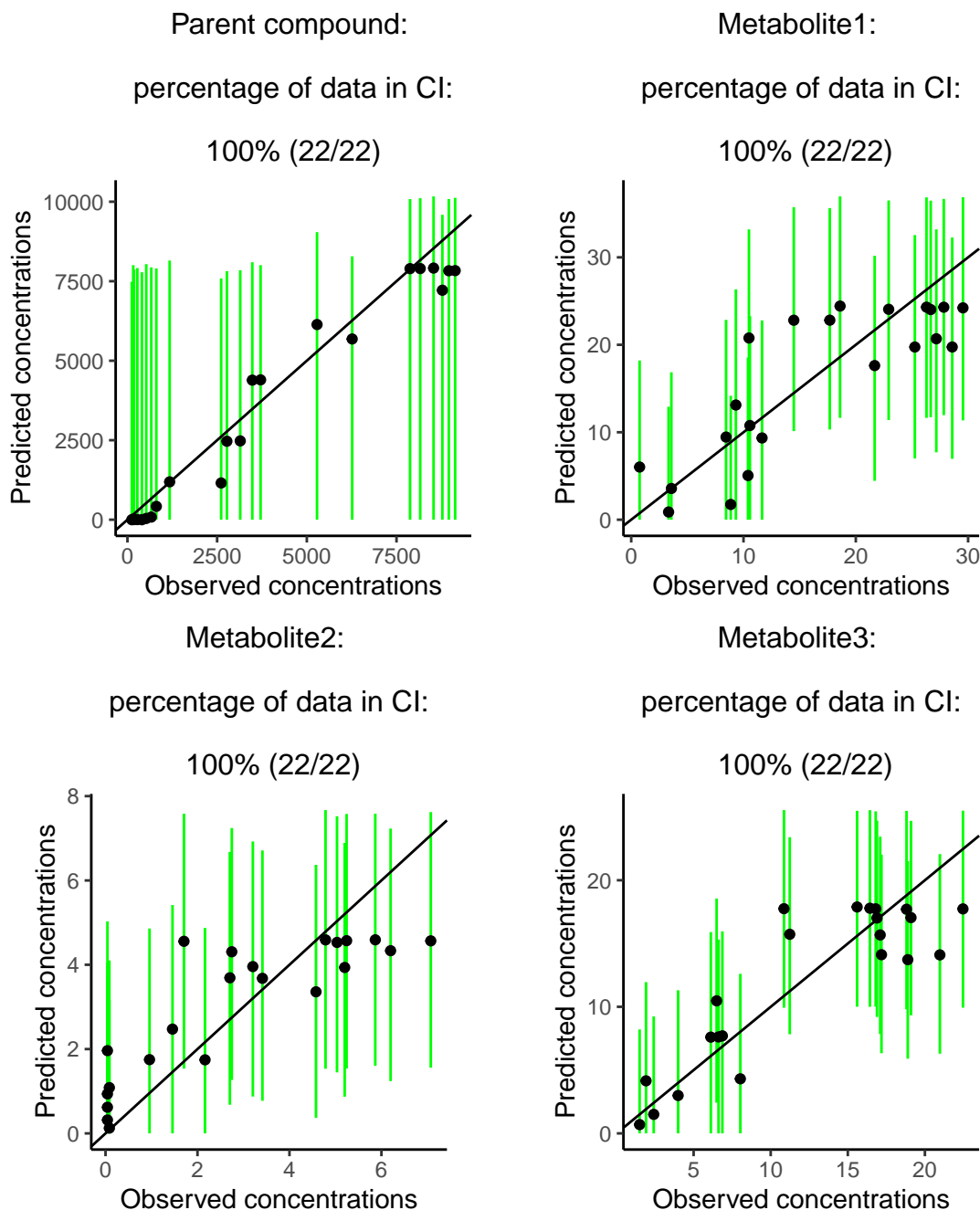
Priors and posteriors

The prior distribution is represented by the gray area and the posterior distribution by the orange area. The accuracy of the model parameter estimation can be visualized by comparing prior and posterior distributions:

the overall expectation is to get a narrower posterior distribution compared to the prior one, what reflects that data contributed enough to precisely estimate parameters.
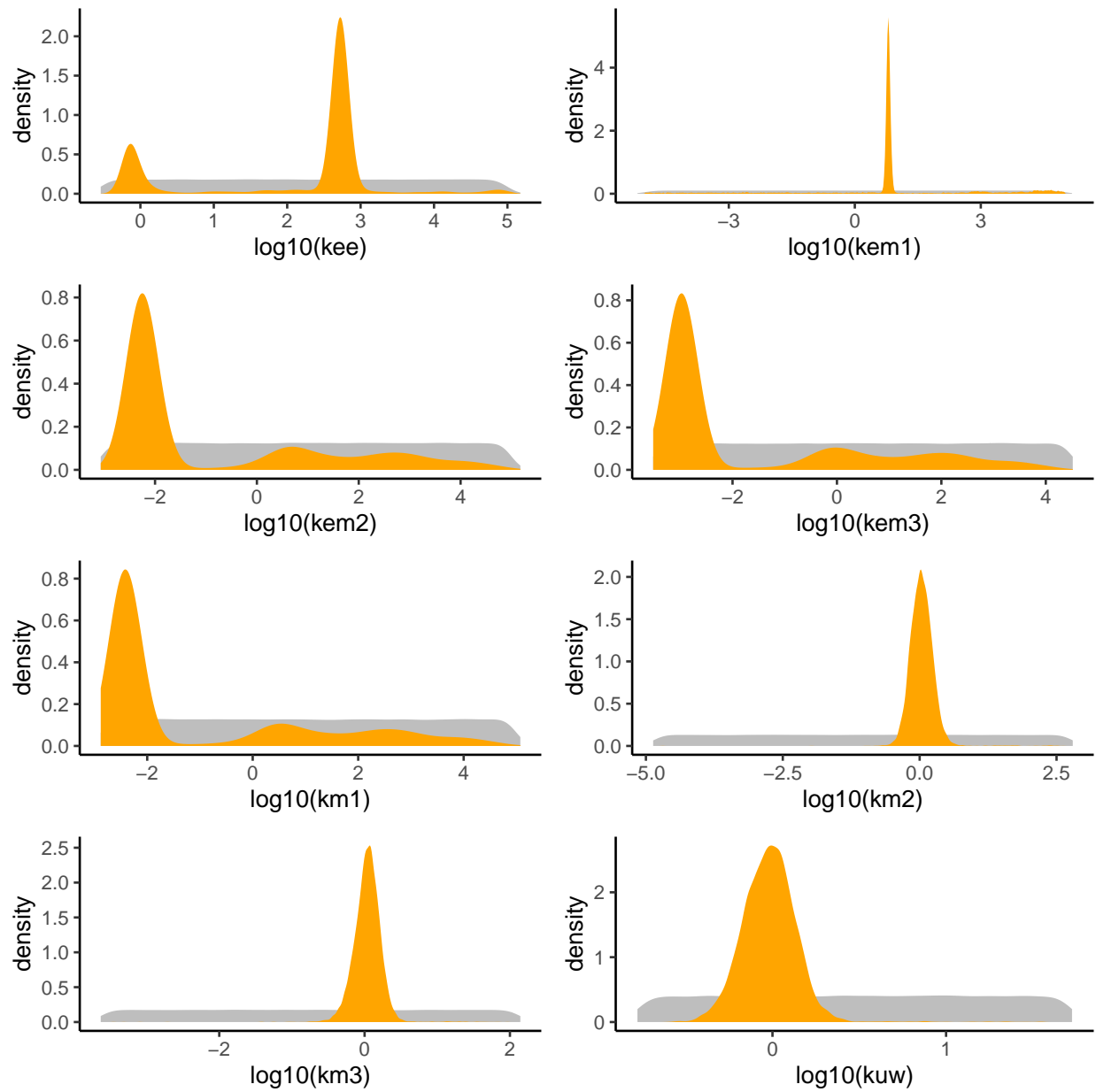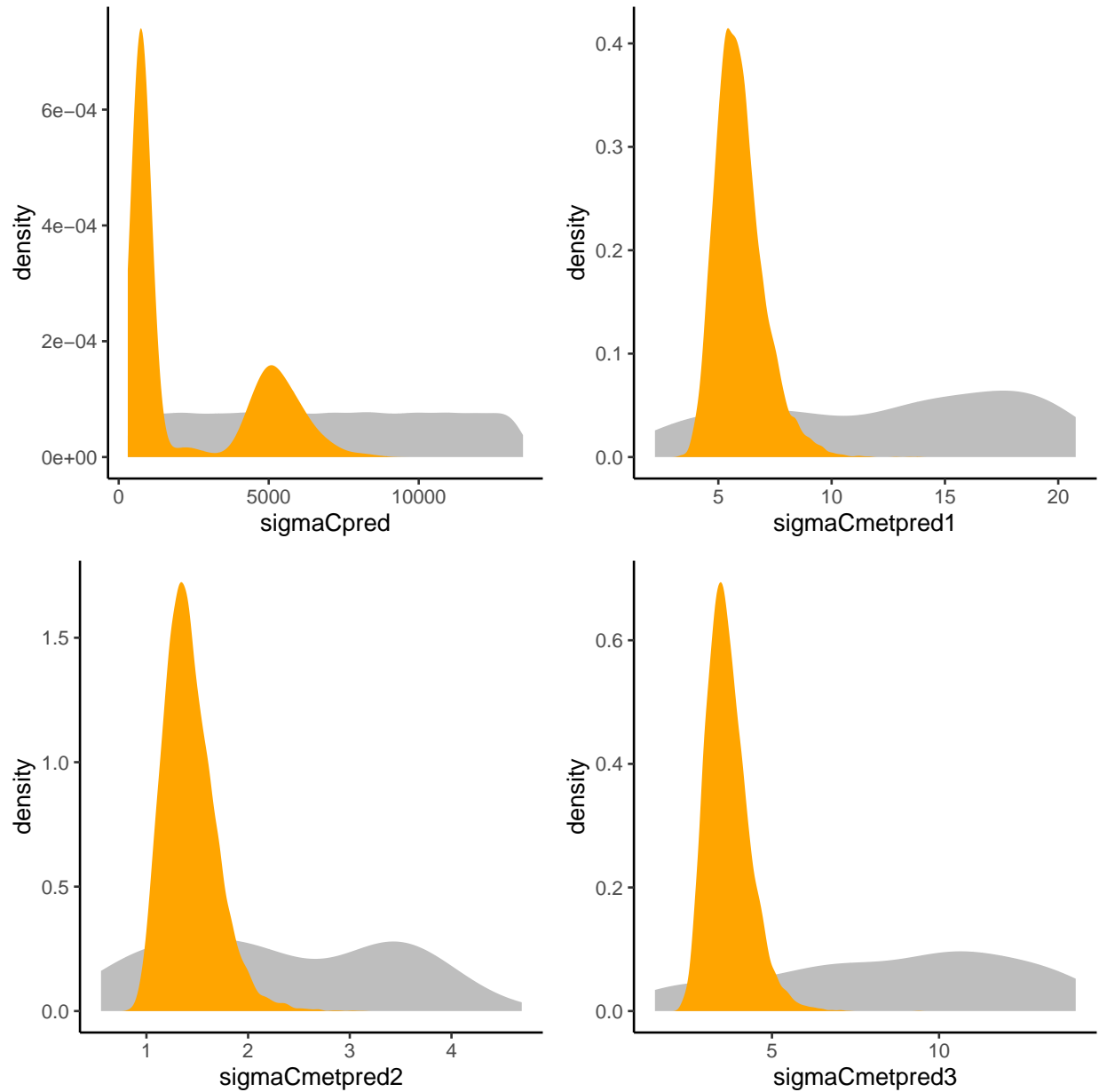
Correlation between parameters

If you want to see the coloured matrix giving a summary of parameter correlations, you need to import the corresponding figure directly from the application, page bottom, section "Downloads", then choose Download an output and select "GOF" then "parameter correlation". You can select the output format you prefer.

Correlations between parameters are visualized by projecting the joint posterior distribution in a plot matrix with planes of parameter pairs (lower triangular elements), marginal posterior distribution of each model parameter (diagonal), and Pearson correlation coefficients (upper triangular elements). Correlations are expected to be low (reflected by "potatoid" shapes of density lines in orange); a leaning elliptical shape translates high correlations (positive if leaning to the right, negative if leaning to the left).
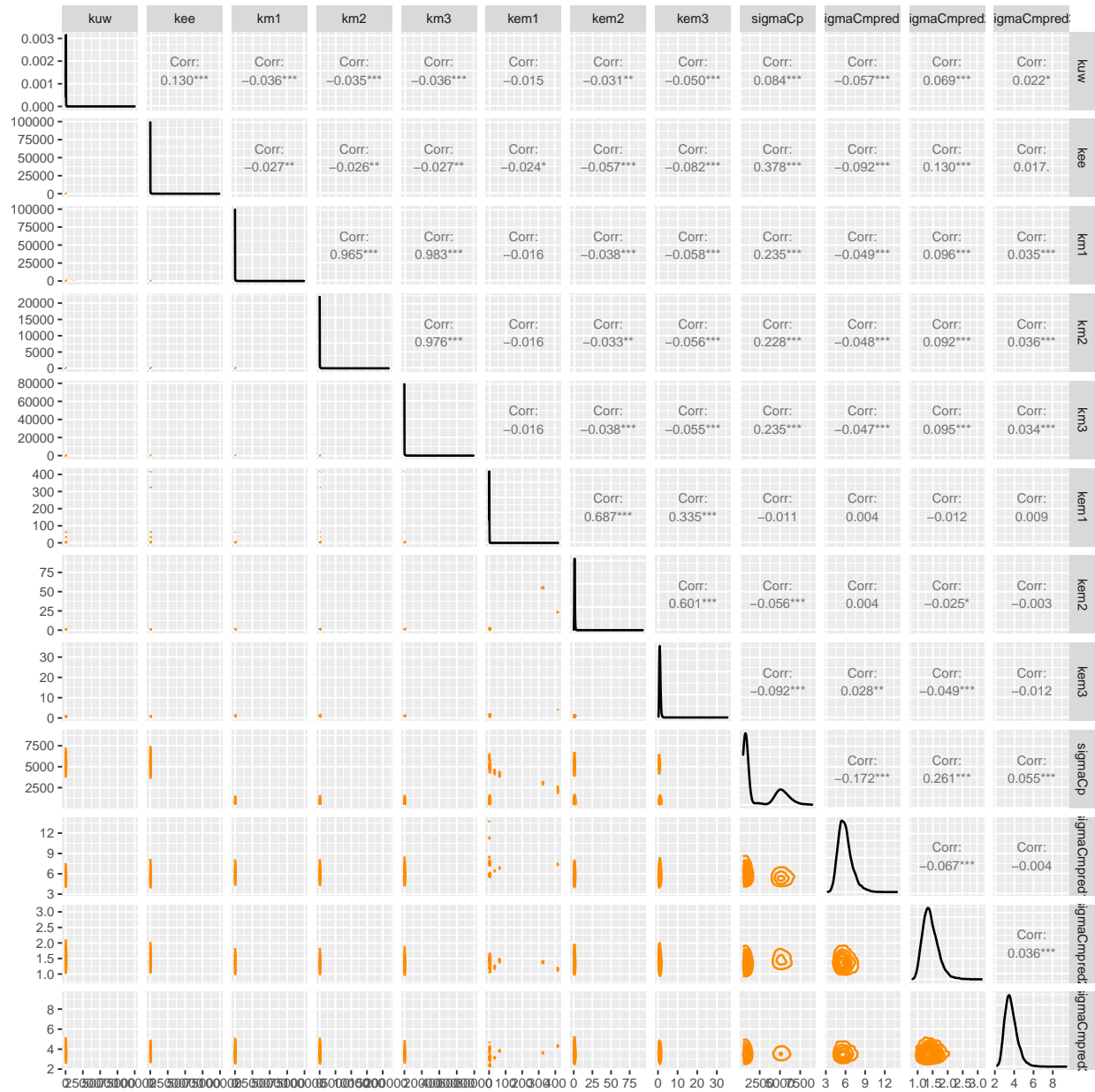
Potential Scale Reduction Factors

Convergence of the MCMC chains can be check with the Gelman-Rubin diagnostic expressed with the potential scale reduction factor (PSRF). Approximate convergence is diagnosed when the PSRF is below 1.01.

	PSRF
kuw	1.332527
kee	1.438268
km1	1.345478
km2	1.342551
km3	1.345721
kem1	1.295563
kem2	1.288564
kem3	1.283668

	PSRF
sigmaCpred	2.18428
sigmaCmetpred1	1.03106
sigmaCmetpred2	1.072077
sigmaCmetpred3	1.002418

Watanabe–Akaike information criterion

Information criteria offer a computationally appealing way of estimating the generalization performance of the model. A fully Bayesian criterion is the widely applicable information criterion (WAIC) by Watanabe a penalized deviance statistics accounting for the uncertainty in the parameters and can be used also for singular models. WAIC is widely used in model comparison for a same dataset (e.g., with or without k_{ee}). Sub-models with lower WAIC values will be preferred.

WAIC = 696.8

Deviance Information Criterion

This criteria, denoted DIC, is a penalized deviance statistics accounting for the number of parameters for use in model comparison for a same dataset (e.g., with or without k_{ee}). Sub-models with lower DIC values will be preferred.
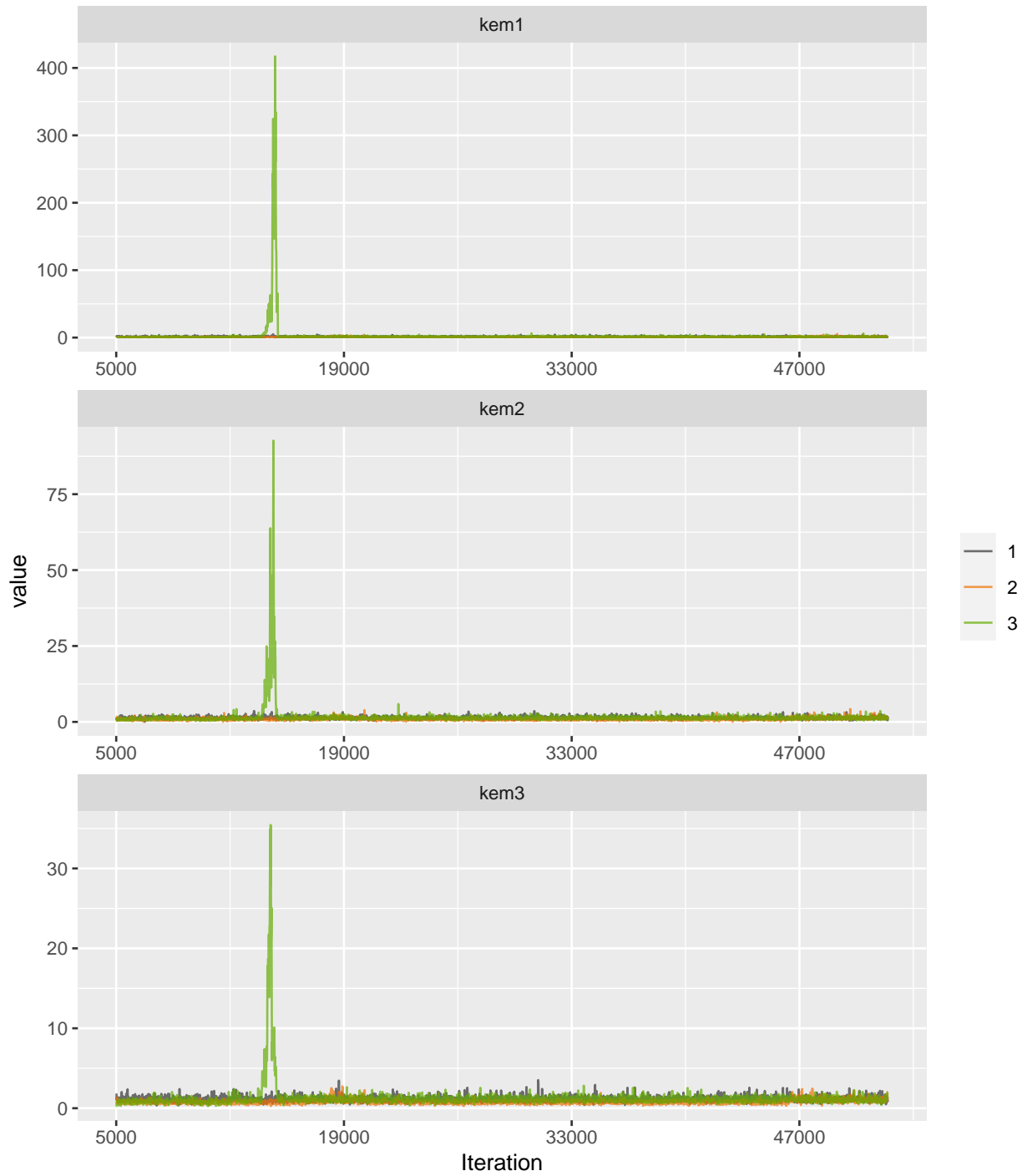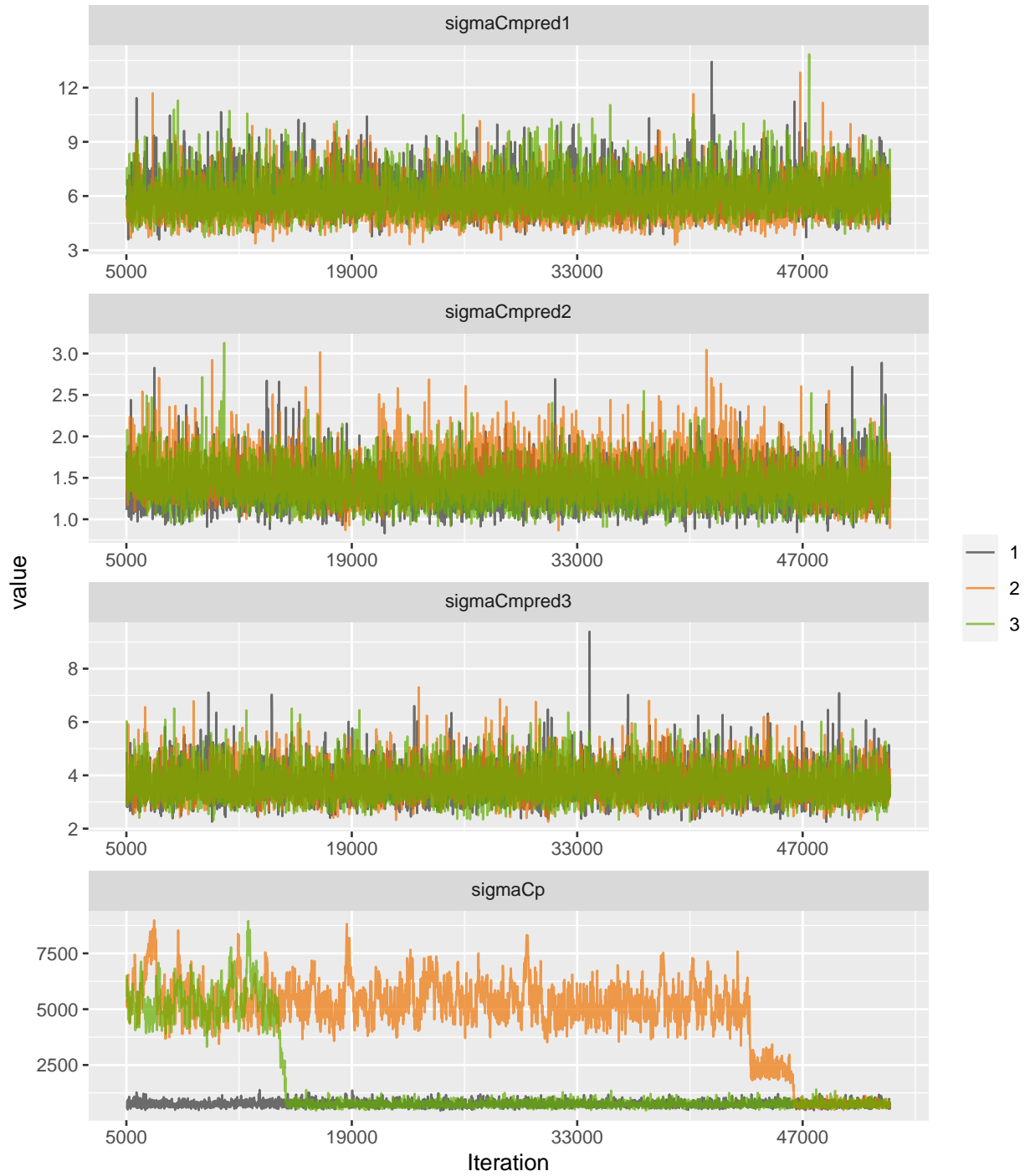
DIC = 1088.247

Traces of MCMC iterations

A traceplot is an essential plot for assessing convergence and diagnosing of MCMC chains. It shows the time series of the sampling process leading to the posterior distribution. Different colors are used for each of the chains (here 3) to assess within-chain convergence.
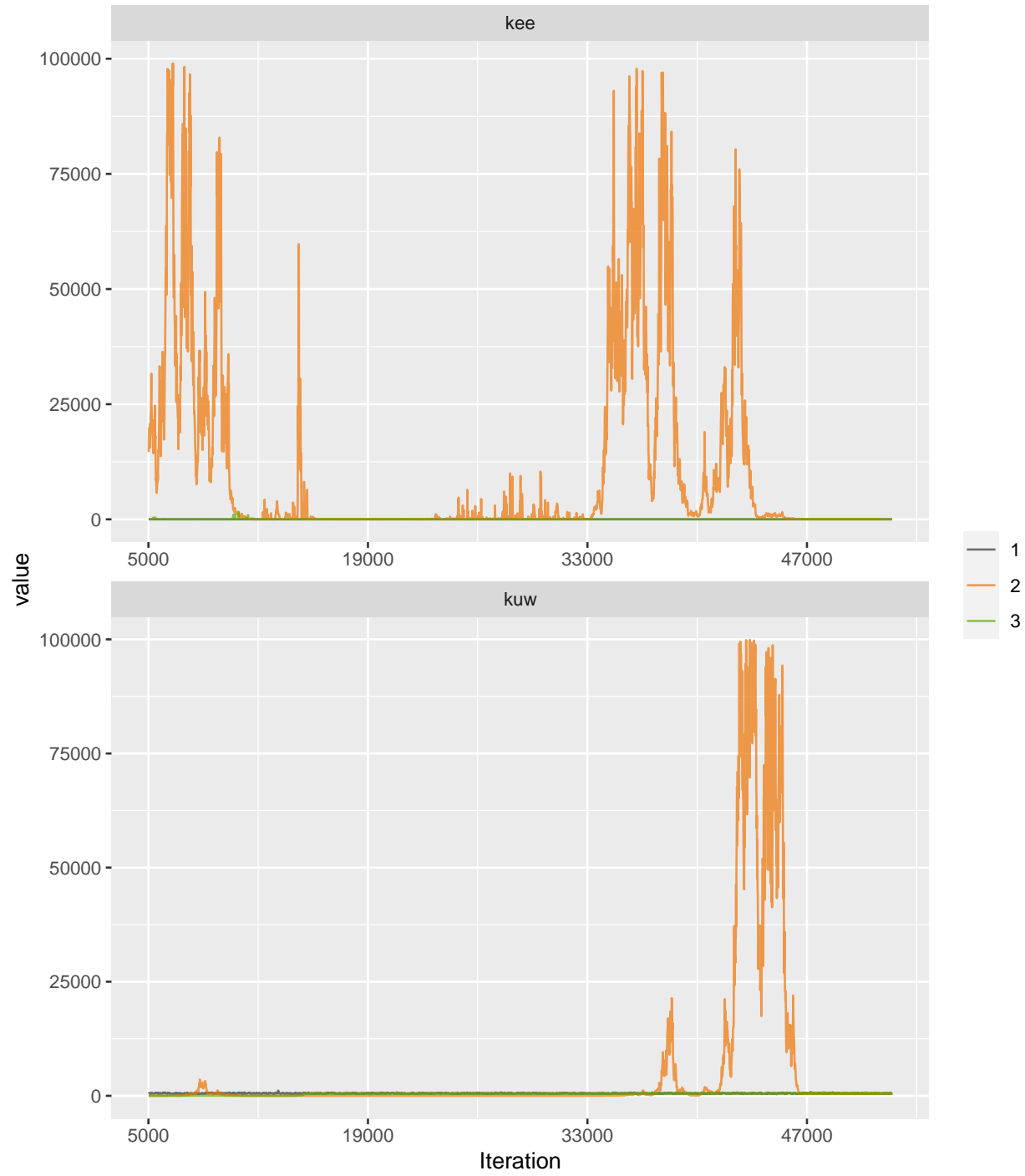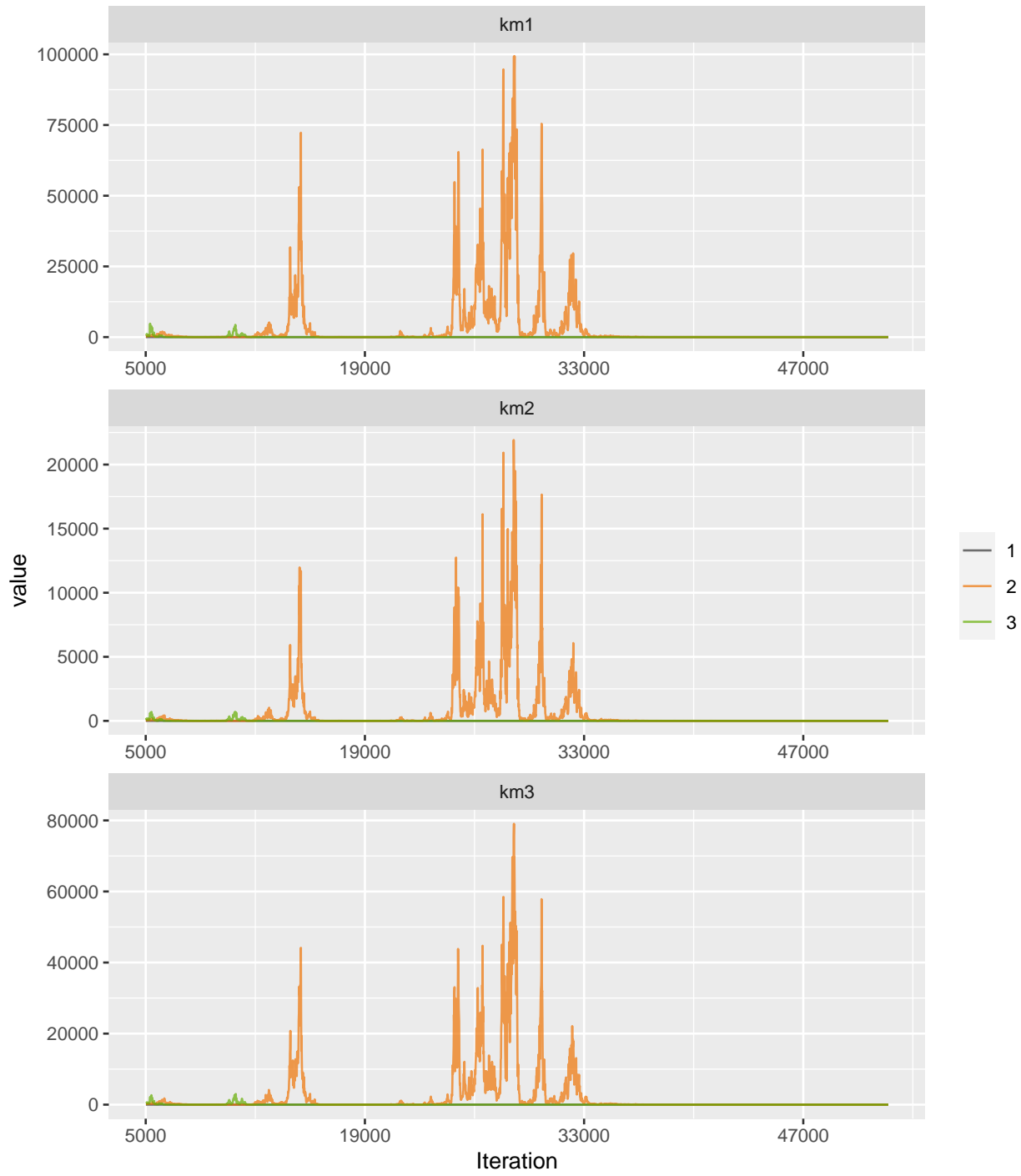
Data Table

time	conc	concm1	concm2	concm3	expw	replicate
0.00	0.0000	0.0000	0.0000	0.0000	100	1
0.04	1099.4930	NA	NA	NA	100	1
0.08	2996.8584	NA	0.0832	NA	100	1
0.08	3085.5109	NA	NA	NA	100	2
0.12	3475.7166	NA	0.0832	NA	100	1
0.12	4362.3089	NA	NA	NA	100	2
0.24	5284.9014	0.7490	0.0832	1.9140	100	1
0.24	6135.9653	4.5354	0.0832	NA	100	2
0.40	8778.5508	10.5687	0.0416	6.6158	100	1
0.75	9134.9810	25.2566	2.7046	17.1845	100	1
0.75	8957.6086	28.5853	3.4119	20.9709	100	2
1.00	8533.4924	18.5992	5.8669	18.8072	100	1
1.00	8161.1520	26.2968	4.7850	16.8100	100	2
1.00	7877.3967	29.5423	1.7060	10.8599	100	3
1.05	6264.1911	27.8363	7.0735	15.6033	100	1
1.05	8250.0067	17.2261	3.2455	NA	100	2
1.09	3711.2019	26.6713	5.2427	16.4355	100	1
1.09	3480.7054	22.9265	5.0347	22.4688	100	2
1.18	3144.2305	14.4799	6.1997	16.8932	100	1
1.18	2771.9575	17.6838	2.7462	19.0985	100	2
1.30	2612.9224	27.1706	3.2039	17.1012	100	1
1.30	1176.8196	10.4854	5.2011	11.2344	100	2
1.46	805.2881	21.6782	4.5770	18.8904	100	1
1.46	521.6002	19.3065	3.6200	NA	100	2
1.75	664.9273	9.3204	1.4563	6.4910	100	1
1.75	132.9450	NA	0.0416	NA	100	2
2.08	524.7013	11.6505	2.1637	6.8655	100	1
2.08	276.5418	8.4466	0.9570	6.1165	100	2
2.71	403.8239	10.4022	0.0416	8.0305	100	1
2.71	120.1359	1.5395	1.5811	NA	100	2
3.10	122.1584	3.5784	0.0416	3.9945	100	1
3.10	122.1584	1.7060	NA	2.5381	100	2
3.95	161.8666	8.8627	0.0416	2.4133	100	1
5.00	184.7882	3.3287	0.0832	1.4979	100	1