Testing hierarchical pathway kinetics with residue data on cyantraniliprole

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Last change on 13 February 2023, last compiled on 13 Februar 2025

Contents

Introduction

The purpose of this document is to test demonstrate how nonlinear hierarchical models (NLHM) based on the parent degradation models SFO, FOMC, DFOP and HS, with serial formation of two or more metabolites can be fitted with the mkin package.

It was assembled in the course of work package 1.2 of Project Number 173340 (Application of nonlinear hierarchical models to the kinetic evaluation of chemical degradation data) of the German Environment Agency carried out in 2022 and 2023.

The mkin package is used in version 1.2.9 which is currently under development. The newly introduced functionality that is used here is a simplification of excluding random effects for a set of fits based on a related set of fits with a reduced model, and the documentation of the starting parameters of the fit, so that all starting parameters of `saem` fits are now listed in the summary. The `saemix` package is used as a backend for fitting the NLHM, but is also loaded to make the convergence plot function available.

This document is processed with the `knitr` package, which also provides the `kable` function that is used to improve the display of tabular data in R markdown documents. For parallel processing, the `parallel` package is used.

```
library(mkin)
library(knitr)
library(saemix)
library(parallel)
n_cores <- detectCores()

# We need to start a new cluster after defining a compiled model that is
# saved as a DLL to the user directory, therefore we define a function
# This is used again after defining the pathway model
start_cluster <- function(n_cores) {
  if (Sys.info()["sysname"] == "Windows") {
    ret <- makePSOCKcluster(n_cores)
  } else {
    ret <- makeForkCluster(n_cores)
  }
  return(ret)
}
cl <- start_cluster(n_cores)
```

Test data

The example data are taken from the final addendum to the DAR from 2014 and are distributed with the mkin package. Residue data and time step normalisation factors are read in using the function `read_spreadsheet` from the mkin package. This function also performs the time step normalisation.

```
data_file <- system.file(
  "testdata", "cyantraniliprole_soil_efsa_2014.xlsx",
  package = "mkin")
cyan_ds <- read_spreadsheet(data_file, parent_only = FALSE)
```

The following tables show the covariate data and the 5 datasets that were read in from the spreadsheet file.

```
pH <- attr(cyan_ds, "covariates")
kable(pH, caption = "Covariate data")
```

Table 1: Covariate data

	pH
Nambsheim	7.90
Tama	6.20
Gross-Umstadt	7.04
Sassafras	4.62
Lleida	8.05

```
for (ds_name in names(cyan_ds)) {
  print(
    kable(mkin_long_to_wide(cyan_ds[[ds_name]]),
      caption = paste("Dataset", ds_name),
      booktabs = TRUE, row.names = FALSE))
    cat("\n\\clearpage\n")
}
```

Table 2: Dataset Nambsheim

time	cyan	JCZ38	J9C38	JSE76	J9Z38
0.000000	105.79	NA	NA	NA	NA
3.210424	77.26	7.92	11.94	5.58	9.12
7.490988	57.13	15.46	16.58	12.59	11.74
17.122259	37.74	15.98	13.36	26.05	10.77
23.543105	31.47	6.05	14.49	34.71	4.96
43.875788	16.74	6.07	7.57	40.38	6.52
67.418893	8.85	10.34	6.39	30.71	8.90
107.014116	5.19	9.61	1.95	20.41	12.93
129.487080	3.45	6.18	1.36	21.78	6.99
195.835832	2.15	9.13	0.95	16.29	7.69
254.693596	1.92	6.92	0.20	13.57	7.16
321.042348	2.26	7.02	NA	11.12	8.66
383.110535	NA	5.05	NA	10.64	5.56
0.000000	105.57	NA	NA	NA	NA
3.210424	78.88	12.77	11.94	5.47	9.12
7.490988	59.94	15.27	16.58	13.60	11.74
17.122259	39.67	14.26	13.36	29.44	10.77
23.543105	30.21	16.07	14.49	35.90	4.96
43.875788	18.06	9.44	7.57	42.30	6.52
67.418893	8.54	5.78	6.39	34.70	8.90
107.014116	7.26	4.54	1.95	23.33	12.93
129.487080	3.60	4.22	1.36	23.56	6.99
195.835832	2.84	3.05	0.95	16.21	7.69
254.693596	2.00	2.90	0.20	15.53	7.16
321.042348	1.79	0.94	NA	9.80	8.66
383.110535	NA	1.82	NA	9.49	5.56

Table 3: Dataset Tama

time	cyan	JCZ38	J9Z38	JSE76
0.000000	106.14	NA	NA	NA
2.400833	93.47	6.46	2.85	NA
5.601943	88.39	10.86	4.65	3.85
12.804442	72.29	11.97	4.91	11.24
17.606108	65.79	13.11	6.63	13.79
32.811382	53.16	11.24	8.90	23.40
50.417490	44.01	11.34	9.98	29.56
80.027761	33.23	8.82	11.31	35.63
96.833591	40.68	5.94	8.32	29.09
146.450803	20.65	4.49	8.72	36.88
190.466072	17.71	4.66	11.10	40.97
240.083284	14.86	2.27	11.62	40.11
286.499386	12.02	NA	10.73	42.58
0.000000	109.11	NA	NA	NA
2.400833	96.84	5.52	2.04	2.02
5.601943	85.29	9.65	2.99	4.39
12.804442	73.68	12.48	5.05	11.47
17.606108	64.89	12.44	6.29	15.00
32.811382	52.27	10.86	7.65	23.30
50.417490	42.61	10.54	9.37	31.06
80.027761	34.29	10.02	9.04	37.87
96.833591	30.50	6.34	8.14	33.97
146.450803	19.21	6.29	8.52	26.15
190.466072	17.55	5.81	9.89	32.08
240.083284	13.22	5.99	10.79	40.66
286.499386	11.09	6.05	8.82	42.90

Table 4: Dataset Gross-Umstadt

time	cyan	JCZ38	J9Z38	JSE76
0.0000000	103.03	NA	NA	NA
2.1014681	87.85	4.79	3.26	0.62
4.9034255	77.35	8.05	9.89	1.32
10.5073404	69.33	9.74	12.32	4.74
21.0146807	55.65	14.57	13.59	9.84
31.5220211	49.03	14.66	16.71	12.32
42.0293615	41.86	15.97	13.64	15.53
63.0440422	34.88	18.20	14.12	22.02
84.0587230	28.26	15.64	14.06	25.60
0.0000000	104.05	NA	NA	NA
2.1014681	85.25	2.68	7.32	0.69
4.9034255	77.22	7.28	8.37	1.45
10.5073404	65.23	10.73	10.93	4.74
21.0146807	57.78	12.29	14.80	9.05
31.5220211	54.83	14.05	12.01	11.05
42.0293615	45.17	12.12	17.89	15.71
63.0440422	34.83	12.90	15.86	22.52
84.0587230	26.59	14.28	14.91	28.48
0.0000000	104.62	NA	NA	NA
0.8145225	97.21	NA	4.00	NA
1.9005525	89.64	3.59	5.24	NA
4.0726125	87.90	4.10	9.58	NA
8.1452251	86.90	5.96	9.45	NA
12.2178376	74.74	7.83	15.03	5.33
16.2904502	74.13	8.84	14.41	5.10
24.4356753	65.26	11.84	18.33	6.71
32.5809004	57.70	12.74	19.93	9.74
0.0000000	101.94	NA	NA	NA
0.8145225	99.94	NA	NA	NA
1.9005525	94.87	NA	4.56	NA
4.0726125	86.96	6.75	6.90	NA
8.1452251	80.51	10.68	7.43	2.58
12.2178376	78.38	10.35	9.46	3.69
16.2904502	70.05	13.73	9.27	7.18
24.4356753	61.28	12.57	13.28	13.19
32.5809004	52.85	12.67	12.95	13.69

Table 5: Dataset Sassafras

time	cyan	JCZ38	J9Z38	JSE76
0.000000	102.17	NA	NA	NA
2.216719	95.49	1.11	0.10	0.83
5.172343	83.35	6.43	2.89	3.30
11.083593	78.18	10.00	5.59	0.81
22.167186	70.44	17.21	4.23	1.09
33.250779	68.00	20.45	5.86	1.17
44.334371	59.64	24.64	3.17	2.72
66.501557	50.73	27.50	6.19	1.27
88.668742	45.65	32.77	5.69	4.54
0.000000	100.43	NA	NA	NA
2.216719	95.34	3.21	0.14	0.46
5.172343	84.38	5.73	4.75	0.62
11.083593	78.50	11.89	3.99	0.73
22.167186	71.17	17.28	4.39	0.66
33.250779	59.41	18.73	11.85	2.65
44.334371	64.57	22.93	5.13	2.01
66.501557	49.08	33.39	5.67	3.63
88.668742	40.41	39.60	5.93	6.17

Table 6: Dataset Lleida

time	cyan	JCZ38	J9Z38	JSE76
0.000000	102.71	NA	NA	NA
2.821051	79.11	5.70	8.07	0.97
6.582451	70.03	7.17	11.31	4.72
14.105253	50.93	10.25	14.84	9.95
28.210505	33.43	10.40	14.82	24.06
42.315758	24.69	9.75	16.38	29.38
56.421010	22.99	10.06	15.51	29.25
84.631516	14.63	5.63	14.74	31.04
112.842021	12.43	4.17	13.53	33.28
0.000000	99.31	NA	NA	NA
2.821051	82.07	6.55	5.60	1.12
6.582451	70.65	7.61	8.01	3.21
14.105253	53.52	11.48	10.82	12.24
28.210505	35.60	11.19	15.43	23.53
42.315758	34.26	11.09	13.26	27.42
56.421010	21.79	4.80	18.30	30.20
84.631516	14.06	6.30	16.35	32.32
112.842021	11.51	5.57	12.64	32.51

Parent only evaluations

As the pathway fits have very long run times, evaluations of the parent data are performed first, in order to determine for each hierarchical parent degradation model which random effects on the degradation model parameters are ill-defined.

```
cyan_sep_const <- mmkin(c("SFO", "FOMC", "DFOP", "SFORB", "HS"),
  cyan_ds, quiet = TRUE, cores = n_cores)
cyan_sep_tc <- update(cyan_sep_const, error_model = "tc")
cyan_saem_full <- mhmkin(list(cyan_sep_const, cyan_sep_tc))
status(cyan_saem_full) |> kable()
```

	const	tc
SFO	OK	OK
FOMC	OK	OK
DFOP	OK	OK
SFORB	OK	OK
HS	OK	OK

All fits converged successfully.

```
illparms(cyan_saem_full) |> kable()
```

	const	tc
SFO	sd(cyan_0)	sd(cyan_0)
FOMC	sd(log_beta)	sd(cyan_0)
DFOP	sd(cyan_0)	sd(cyan_0), sd(log_k1)
SFORB	sd(cyan_free_0)	sd(cyan_free_0), sd(log_k_cyan_free_bound)
HS	sd(cyan_0)	sd(cyan_0)

In almost all models, the random effect for the initial concentration of the parent compound is ill-defined. For the biexponential models DFOP and SFORB, the random effect of one additional parameter is ill-defined when the two-component error model is used.

```
anova(cyan_saem_full) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
SFO const	5	833.9	832.0	-412.0
SFO tc	6	831.6	829.3	-409.8
FOMC const	7	709.1	706.4	-347.6
FOMC tc	8	689.2	686.1	-336.6
DFOP const	9	703.0	699.5	-342.5
SFORB const	9	701.3	697.8	-341.7
HS const	9	718.6	715.1	-350.3
DFOP tc	10	703.1	699.2	-341.6
SFORB tc	10	700.0	696.1	-340.0
HS tc	10	716.7	712.8	-348.3

Model comparison based on AIC and BIC indicates that the two-component error model is preferable for all parent models with the exception of DFOP. The lowest AIC and BIC values are are obtained with the FOMC model, followed by SFORB and DFOP.

```
stopCluster(cl)
```

Pathway fits

Evaluations with pathway established previously

To test the technical feasibility of coupling the relevant parent degradation models with different transformation pathway models, a list of `mkinmod` models is set up below. As in the EU evaluation, parallel formation of metabolites JCZ38 and J9Z38 and secondary formation of metabolite JSE76 from JCZ38 is used.

```
if (!dir.exists("cyan_dlls")) dir.create("cyan_dlls")
cyan_path_1 <- list(
  sfo_path_1 = mkinmod(
    cyan = mkinsub("SFO", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SFO", "JSE76"),
    J9Z38 = mkinsub("SFO"),
    JSE76 = mkinsub("SFO"), quiet = TRUE,
    name = "sfo_path_1", dll_dir = "cyan_dlls", overwrite = TRUE),
  fomc_path_1 = mkinmod(
    cyan = mkinsub("FOMC", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SFO", "JSE76"),
    J9Z38 = mkinsub("SFO"),
    JSE76 = mkinsub("SFO"), quiet = TRUE,
    name = "fomc_path_1", dll_dir = "cyan_dlls", overwrite = TRUE),
  dfop_path_1 = mkinmod(
    cyan = mkinsub("DFOP", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SFO", "JSE76"),
    J9Z38 = mkinsub("SFO"),
    JSE76 = mkinsub("SFO"), quiet = TRUE,
    name = "dfop_path_1", dll_dir = "cyan_dlls", overwrite = TRUE),
  sforb_path_1 = mkinmod(
    cyan = mkinsub("SFORB", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SFO", "JSE76"),
    J9Z38 = mkinsub("SFO"),
    JSE76 = mkinsub("SFO"), quiet = TRUE,
    name = "sforb_path_1", dll_dir = "cyan_dlls", overwrite = TRUE),
  hs_path_1 = mkinmod(
    cyan = mkinsub("HS", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SFO", "JSE76"),
    J9Z38 = mkinsub("SFO"),
    JSE76 = mkinsub("SFO"), quiet = TRUE,
    name = "hs_path_1", dll_dir = "cyan_dlls", overwrite = TRUE)
)
cl_path_1 <- start_cluster(n_cores)
```

To obtain suitable starting values for the NLHM fits, separate pathway fits are performed for all datasets.

```
f_sep_1_const <- mmkin(
  cyan_path_1,
  cyan_ds,
  error_model = "const",
  cluster = cl_path_1,
  quiet = TRUE)
status(f_sep_1_const) |> kable()
```

	Nambsheim	Tama	Gross-Umstadt	Sassafras	Lleida
sfo_path_1	OK	OK	OK	C	OK
fomc_path_1	OK	OK	OK	OK	OK
dfop_path_1	OK	OK	OK	OK	OK

	Nambsheim	Tama	Gross-Umstadt	Sassafras	Lleida
sforb_path_1	OK	OK	OK	OK	OK
hs_path_1	C	C	C	C	C

```
f_sep_1_tc <- update(f_sep_1_const, error_model = "tc")
status(f_sep_1_tc) |> kable()
```

	Nambsheim	Tama	Gross-Umstadt	Sassafras	Lleida
sfo_path_1	OK	OK	OK	OK	OK
fomc_path_1	OK	OK	OK	OK	OK
dfop_path_1	OK	OK	OK	OK	OK
sforb_path_1	OK	OK	OK	OK	OK
hs_path_1	C	OK	C	OK	C

Most separate fits converged successfully. The biggest convergence problems are seen when using the HS model with constant variance.

For the hierarchical pathway fits, those random effects that could not be quantified in the corresponding parent data analyses are excluded.

In the code below, the output of the `illparms` function for the parent only fits is used as an argument `no_random_effect` to the `mhmkin` function. The possibility to do so was introduced in mkin version `1.2.2` which is currently under development.

```
f_saem_1 <- mhmkin(list(f_sep_1_const, f_sep_1_tc),
  no_random_effect = illparms(cyan_saem_full),
  cluster = cl_path_1)
```

```
status(f_saem_1) |> kable()
```

	const	tc
sfo_path_1	FO	Fth, FO
fomc_path_1	OK	Fth, FO
dfop_path_1	Fth, FO	Fth, FO
sforb_path_1	Fth, FO	Fth, FO
hs_path_1	FO	E

The status information from the individual fits shows that all fits completed successfully. The matrix entries Fth and FO indicate that the Fisher Information Matrix could not be inverted for the fixed effects (theta) and the random effects (Omega), respectively. For the affected fits, ill-defined parameters cannot be determined using the `illparms` function, because it relies on the Fisher Information Matrix.

```
illparms(f_saem_1) |> kable()
```

	const	tc
sfo_path_1	NA	NA
fomc_path_1	sd(log_k_J9Z38), sd(f_cyan_ilr_2), sd(f_JCZ38_qlogis)	NA
dfop_path_1	NA	NA
sforb_path_1	NA	NA
hs_path_1	NA	E

The model comparisons below suggest that the pathway fits using DFOP or SFORB for the parent compound provide the best fit.

```
anova(f_saem_1[, "const"]) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
sfo_path_1 const	16	2693.0	2686.8	-1330.5
fomc_path_1 const	18	2427.9	2420.9	-1196.0
dfop_path_1 const	20	2403.2	2395.4	-1181.6
sforb_path_1 const	20	2401.4	2393.6	-1180.7
hs_path_1 const	20	2427.2	2419.4	-1193.6

```
anova(f_saem_1[1:4, ]) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
sfo_path_1 const	16	2693.0	2686.8	-1330.5
sfo_path_1 tc	17	2657.6	2651.0	-1311.8
fomc_path_1 const	18	2427.9	2420.9	-1196.0
fomc_path_1 tc	19	2423.6	2416.2	-1192.8
dfop_path_1 const	20	2403.2	2395.4	-1181.6
sforb_path_1 const	20	2401.4	2393.6	-1180.7
dfop_path_1 tc	20	2398.0	2390.1	-1179.0
sforb_path_1 tc	20	2399.9	2392.1	-1180.0

For these two parent model, successful fits are shown below. Plots of the fits with the other parent models are shown in the Appendix.

```
plot(f_saem_1[["dfop_path_1", "tc"]])
```

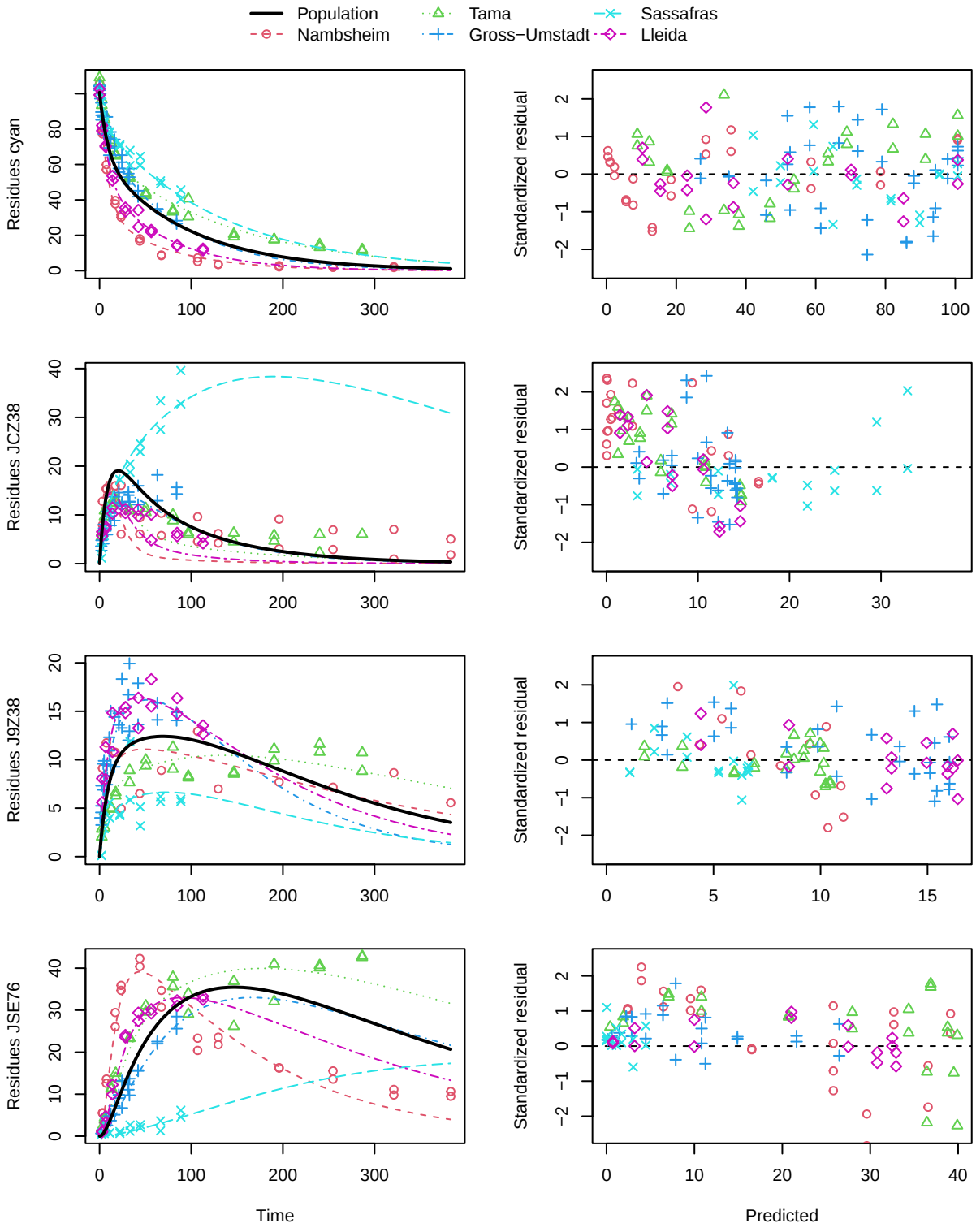

Figure 1: DFOP pathway fit with two-component error

```
plot(f_saem_1[["sforb_path_1", "tc"]])
```

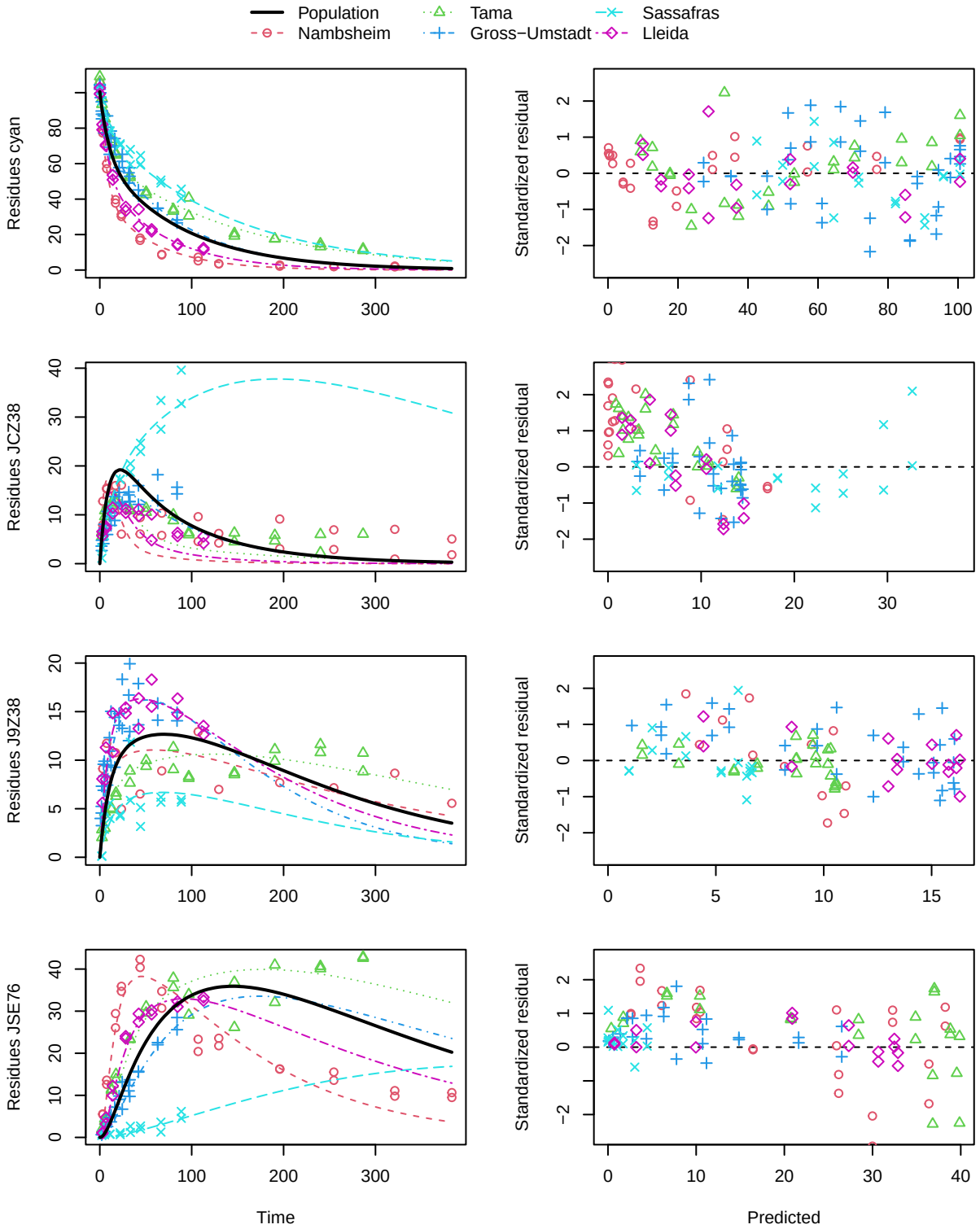

Figure 2: SFORB pathway fit with two-component error

A closer graphical analysis of these Figures shows that the residues of transformation product JCZ38 in the soils Tama and Nambsheim observed at later time points are strongly and systematically underestimated.

```
stopCluster(cl_path_1)
```

Alternative pathway fits

To improve the fit for JCZ38, a back-reaction from JSE76 to JCZ38 was introduced in an alternative version of the transformation pathway, in analogy to the back-reaction from K5A78 to K5A77. Both pairs of transformation products are pairs of an organic acid with its corresponding amide (Addendum 2014, p. 109). As FOMC provided the best fit for the parent, and the biexponential models DFOP and SFORB provided the best initial pathway fits, these three parent models are used in the alternative pathway fits.

```
cyan_path_2 <- list(
  fomc_path_2 = mkinmod(
    cyan = mkinsub("FOMC", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SFO", "JSE76"),
    J9Z38 = mkinsub("SFO"),
    JSE76 = mkinsub("SFO", "JCZ38"),
    name = "fomc_path_2", quiet = TRUE,
    dll_dir = "cyan_dlls",
    overwrite = TRUE
  ),
  dfop_path_2 = mkinmod(
    cyan = mkinsub("DFOP", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SFO", "JSE76"),
    J9Z38 = mkinsub("SFO"),
    JSE76 = mkinsub("SFO", "JCZ38"),
    name = "dfop_path_2", quiet = TRUE,
    dll_dir = "cyan_dlls",
    overwrite = TRUE
  ),
  sforb_path_2 = mkinmod(
    cyan = mkinsub("SFORB", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SFO", "JSE76"),
    J9Z38 = mkinsub("SFO"),
    JSE76 = mkinsub("SFO", "JCZ38"),
    name = "sforb_path_2", quiet = TRUE,
    dll_dir = "cyan_dlls",
    overwrite = TRUE
  )
)

cl_path_2 <- start_cluster(n_cores)
f_sep_2_const <- mmkin(
  cyan_path_2,
  cyan_ds,
  error_model = "const",
  cluster = cl_path_2,
  quiet = TRUE)

status(f_sep_2_const) |> kable()
```

	Nambsheim	Tama	Gross-Umstadt	Sassafras	Lleida
fomc_path_2	OK	OK	OK	C	OK
dfop_path_2	OK	OK	OK	C	OK
sforb_path_2	OK	OK	OK	OK	OK

Using constant variance, separate fits converge with the exception of the fits to the Sassafras soil data.

```
f_sep_2_tc <- update(f_sep_2_const, error_model = "tc")
status(f_sep_2_tc) |> kable()
```

	Nambsheim	Tama	Gross-Umstadt	Sassafras	Lleida
fomc_path_2	OK	OK	OK	C	OK
dfop_path_2	OK	C	OK	C	OK
sforb_path_2	OK	OK	OK	C	OK

Using the two-component error model, all separate fits converge with the exception of the alternative pathway fit with DFOP used for the parent and the Sassafras dataset.

```
f_saem_2 <- mhmkin(list(f_sep_2_const, f_sep_2_tc),
  no_random_effect = illparms(cyan_saem_full[2:4, ]),
  cluster = cl_path_2)
```

```
status(f_saem_2) |> kable()
```

	const	tc
fomc_path_2	E	OK
dfop_path_2	OK	OK
sforb_path_2	OK	OK

The hierarchical fits for the alternative pathway completed successfully, with the exception of the model using FOMC for the parent compound and constant variance as the error model.

```
illparms(f_saem_2) |> kable()
```

	const	tc
fomc_path_2	E	sd(f_JSE76_qlogis)
dfop_path_2	sd(f_JCZ38_qlogis), sd(f_JSE76_qlogis)	sd(f_JCZ38_qlogis), sd(f_JSE76_qlogis)
sforb_path_2	sd(f_JCZ38_qlogis), sd(f_JSE76_qlogis)	sd(f_JCZ38_qlogis), sd(f_JSE76_qlogis)

In all biphasic fits (DFOP or SFORB for the parent compound), the random effects for the formation fractions for the pathways from JCZ38 to JSE76, and for the reverse pathway from JSE76 to JCZ38 are ill-defined.

```
anova(f_saem_2[, "tc"]) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
fomc_path_2 tc	21	2249.0	2240.8	-1103.5
dfop_path_2 tc	22	2234.4	2225.8	-1095.2
sforb_path_2 tc	22	2239.7	2231.1	-1097.9

```
anova(f_saem_2[2:3,]) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
dfop_path_2 const	22	2288.4	2279.8	-1122.2
sforb_path_2 const	22	2283.3	2274.7	-1119.7
dfop_path_2 tc	22	2234.4	2225.8	-1095.2
sforb_path_2 tc	22	2239.7	2231.1	-1097.9

The variants using the biexponential models DFOP and SFORB for the parent compound and the two-component error model give the lowest AIC and BIC values and are plotted below. Compared with the original pathway, the AIC and BIC values indicate a large improvement. This is confirmed by the plots, which show that the metabolite JCZ38 is fitted much better with this model.

```
plot(f_saem_2[["fomc_path_2", "tc"]])
```

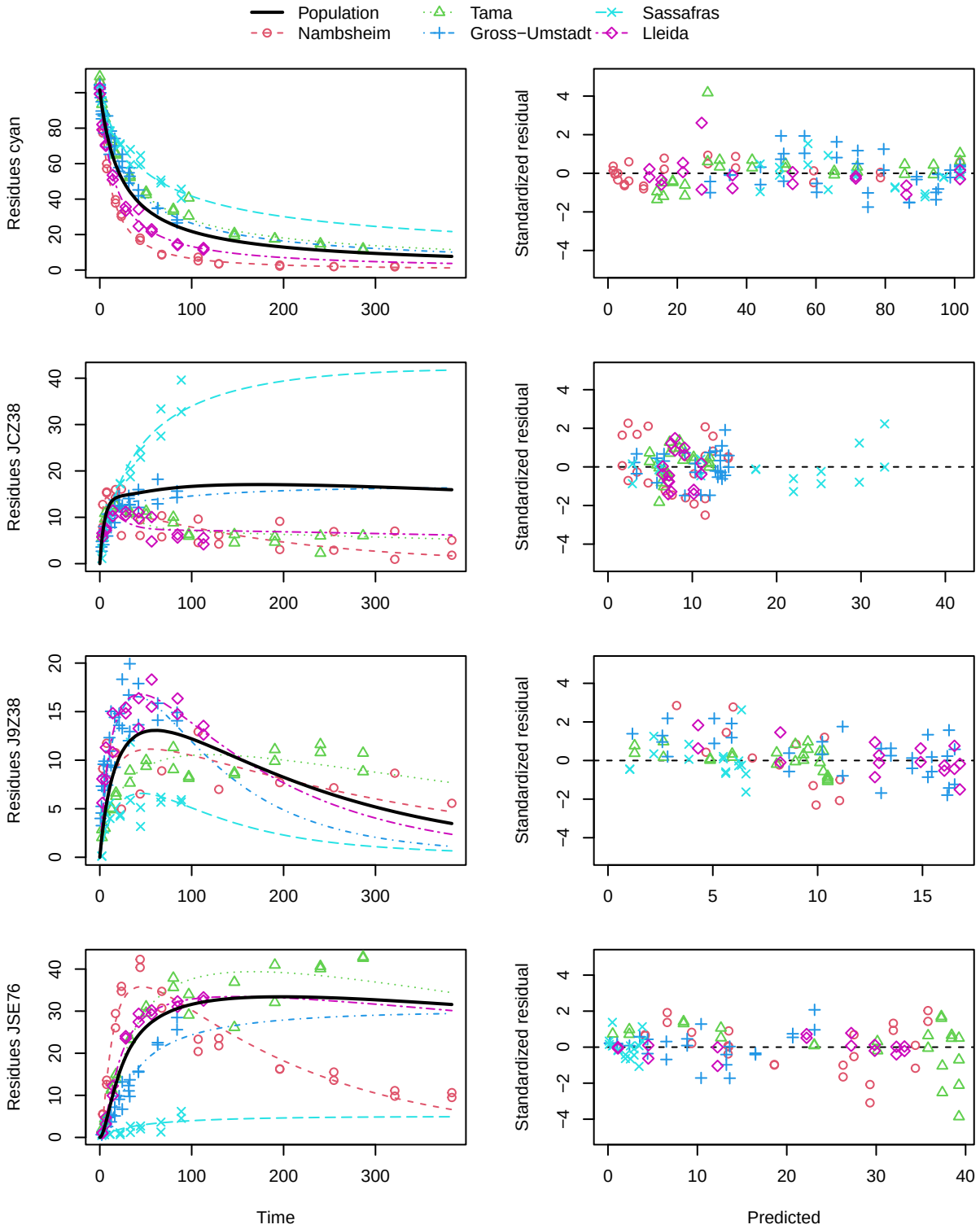

Figure 3: FOMC pathway fit with two-component error, alternative pathway

```
plot(f_saem_2[["dfop_path_2", "tc"]])
```

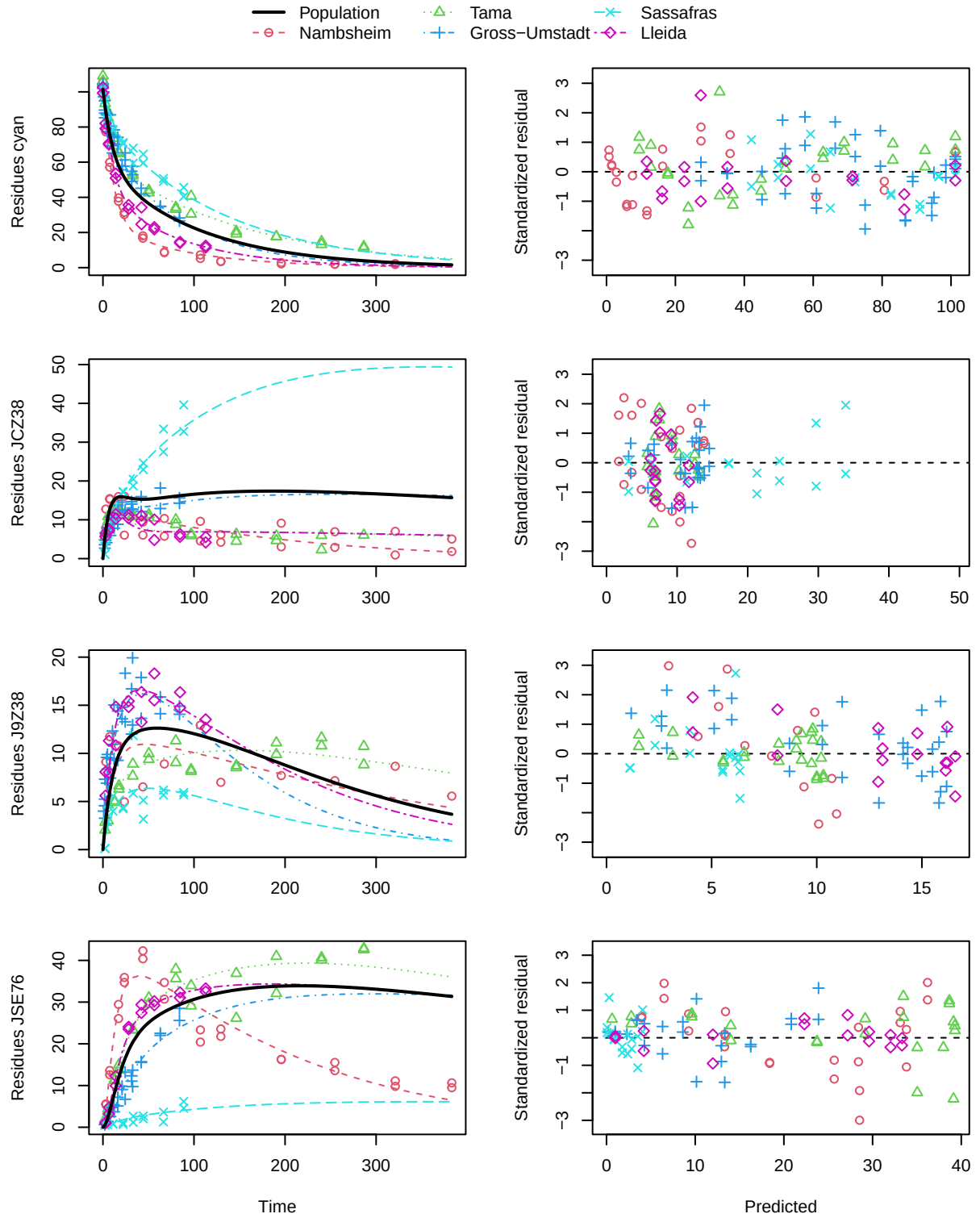

Figure 4: DFOP pathway fit with two-component error, alternative pathway

```
plot(f_saem_2[["sforb_path_2", "tc"]])
```

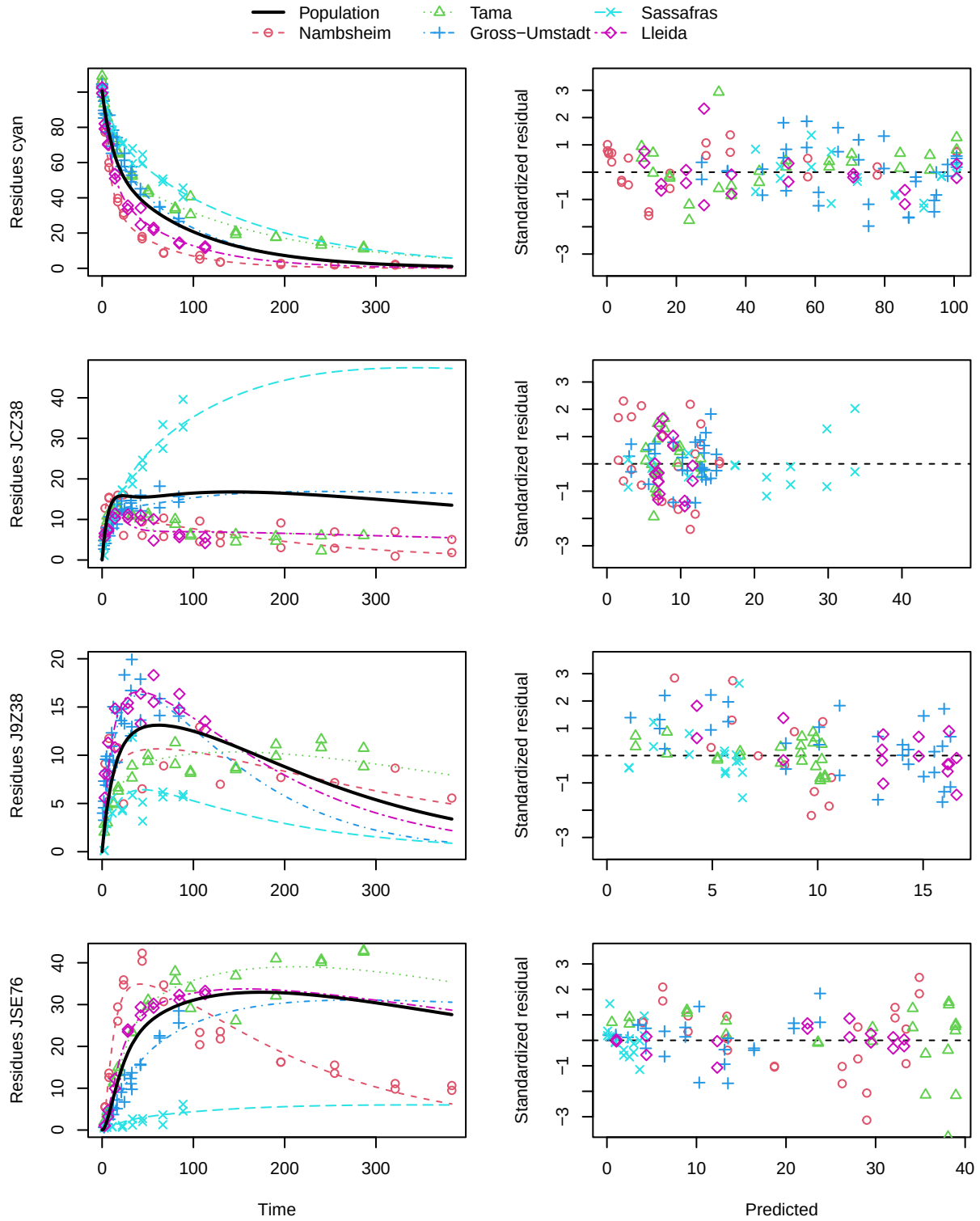

Figure 5: SFORB pathway fit with two-component error, alternative pathway

Refinement of alternative pathway fits

All ill-defined random effects that were identified in the parent only fits and in the above pathway fits, are excluded for the final evaluations below. For this purpose, a list of character vectors is created below that can be indexed by row and column indices, and which contains the degradation parameter names for which random effects should be excluded for each of the hierarchical fits contained in `f_saem_2`.

```
no_ranef <- matrix(list(), nrow = 3, ncol = 2, dimnames = dimnames(f_saem_2))
no_ranef[["fomc_path_2", "const"]] <- c("log_beta", "f_JCZ38_qlogis", "f_JSE76_qlogis")
no_ranef[["fomc_path_2", "tc"]] <- c("cyan_0", "f_JCZ38_qlogis", "f_JSE76_qlogis")
no_ranef[["dfop_path_2", "const"]] <- c("cyan_0", "f_JCZ38_qlogis", "f_JSE76_qlogis")
no_ranef[["dfop_path_2", "tc"]] <- c("cyan_0", "log_k1", "f_JCZ38_qlogis", "f_JSE76_qlogis")
no_ranef[["sforb_path_2", "const"]] <- c("cyan_free_0",
  "f_JCZ38_qlogis", "f_JSE76_qlogis")
no_ranef[["sforb_path_2", "tc"]] <- c("cyan_free_0", "log_k_cyan_free_bound",
  "f_JCZ38_qlogis", "f_JSE76_qlogis")
clusterExport(cl_path_2, "no_ranef")

f_saem_3 <- update(f_saem_2,
  no_random_effect = no_ranef,
  cluster = cl_path_2)
```

```
status(f_saem_3) |> kable()
```

	const	tc
fomc_path_2	E	Fth
dfop_path_2	Fth	Fth
sforb_path_2	Fth	Fth

With the exception of the FOMC pathway fit with constant variance, all updated fits completed successfully. However, the Fisher Information Matrix for the fixed effects (Fth) could not be inverted, so no confidence intervals for the optimised parameters are available.

```
illparms(f_saem_3) |> kable()
```

	const	tc
fomc_path_2	E	
dfop_path_2		
sforb_path_2		

```
anova(f_saem_3[, "tc"]) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
fomc_path_2 tc	19	2249.1	2241.6	-1105.5
dfop_path_2 tc	20	2237.3	2229.5	-1098.6
sforb_path_2 tc	20	2241.3	2233.5	-1100.7

```
anova(f_saem_3[2:3,]) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
dfop_path_2 const	20	2282.2	2274.4	-1121.1
sforb_path_2 const	20	2279.7	2271.9	-1119.9

	npar	AIC	BIC	Lik
dfop_path_2 tc	20	2237.3	2229.5	-1098.6
sforb_path_2 tc	20	2241.3	2233.5	-1100.7

While the AIC and BIC values of the best fit (DFOP pathway fit with two-component error) are lower than in the previous fits with the alternative pathway, the practical value of these refined evaluations is limited as no confidence intervals are obtained.

```
stopCluster(cl_path_2)
```

Conclusion

It was demonstrated that a relatively complex transformation pathway with parallel formation of two primary metabolites and one secondary metabolite can be fitted even if the data in the individual datasets are quite different and partly only cover the formation phase.

The run times of the pathway fits were several hours, limiting the practical feasibility of iterative refinements based on ill-defined parameters and of alternative checks of parameter identifiability based on multistart runs.

Acknowledgements

The helpful comments by Janina Wöltjen of the German Environment Agency are gratefully acknowledged.

Appendix

Plots of fits that were not refined further

```
plot(f_saem_1[["sfo_path_1", "tc"]])
```

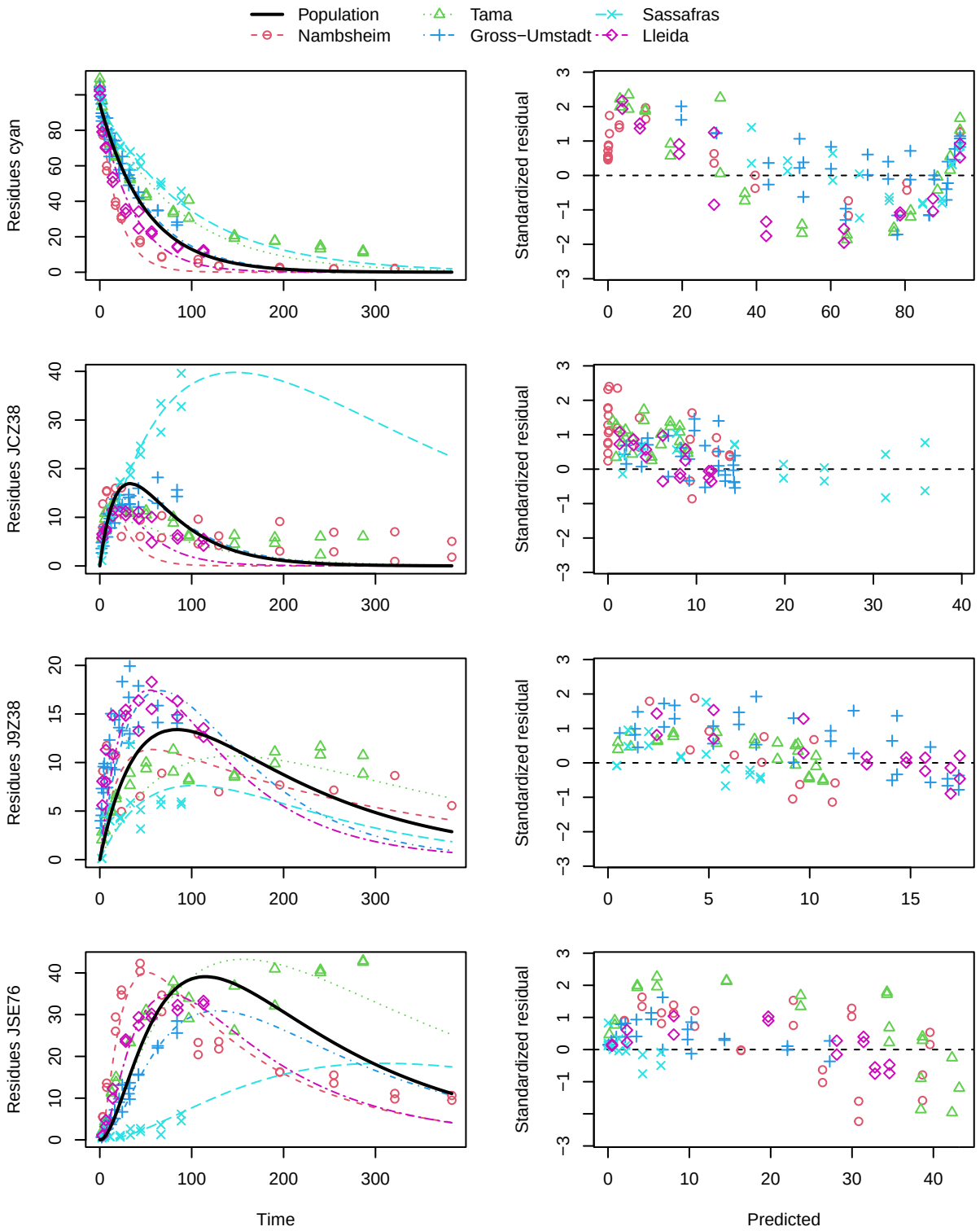

Figure 6: SFO pathway fit with two-component error

```
plot(f_saem_1[["fomc_path_1", "tc"]])
```

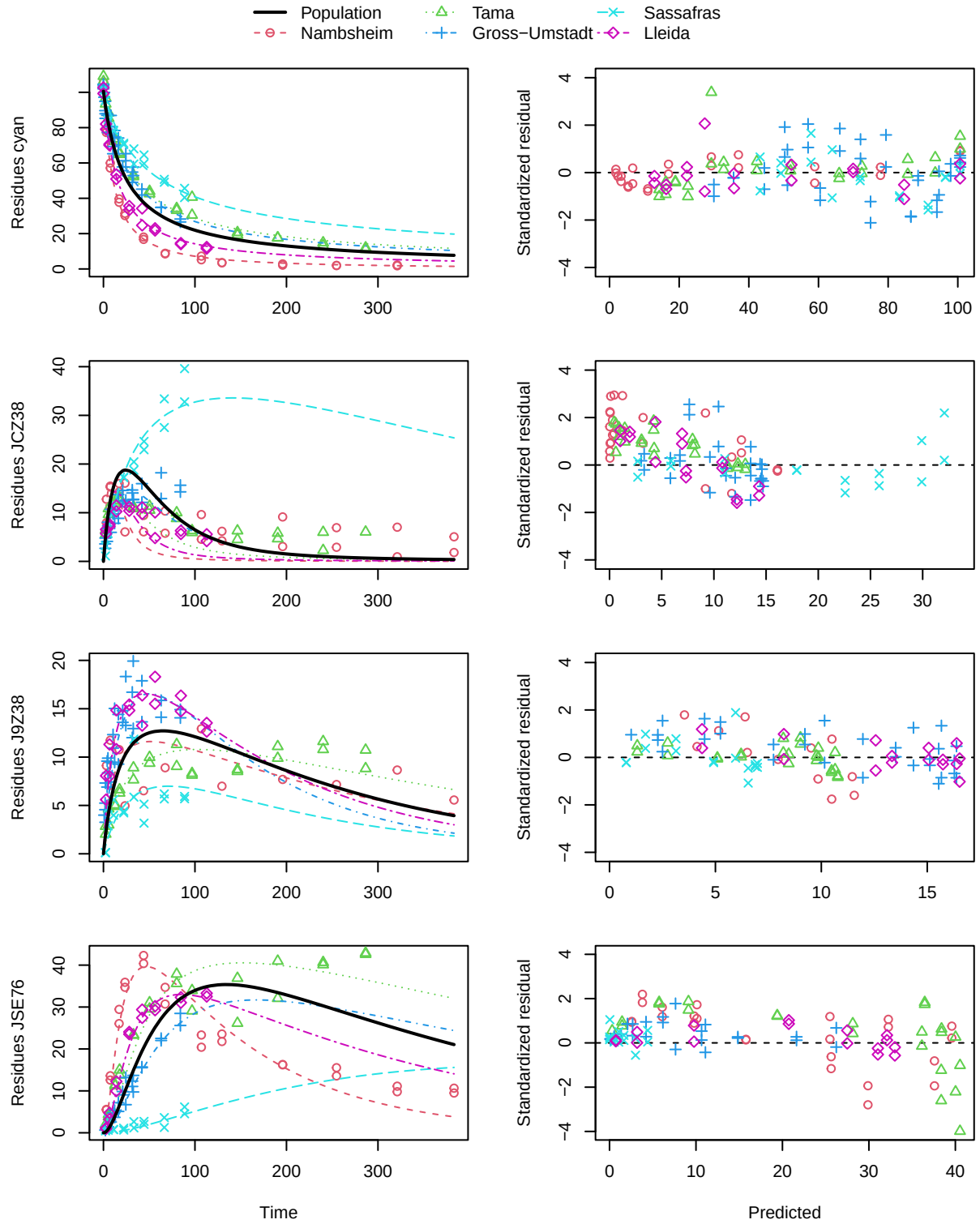

Figure 7: FOMC pathway fit with two-component error

```
plot(f_saem_1[["sforb_path_1", "tc"]])
```

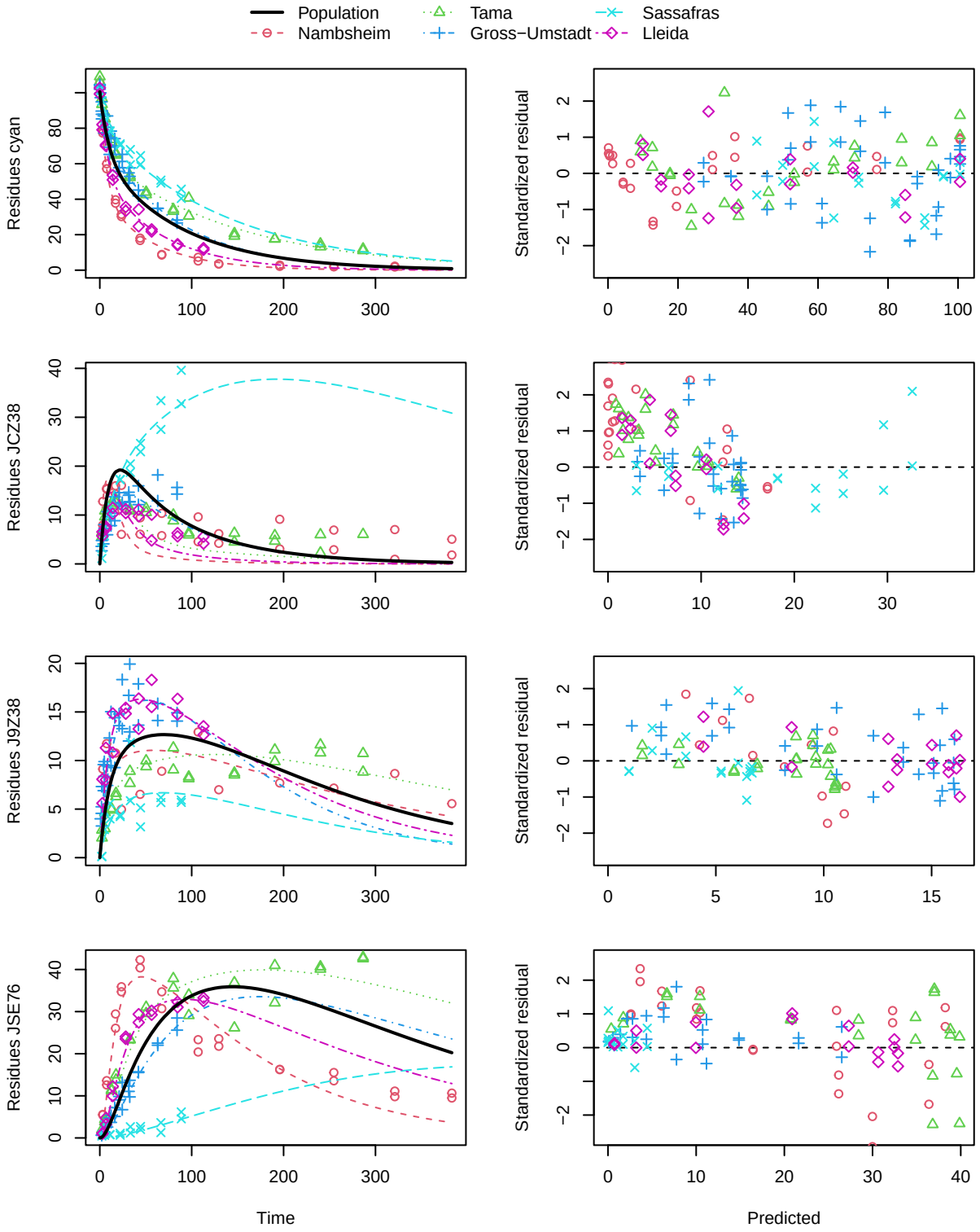

Figure 8: HS pathway fit with two-component error

Hierarchical fit listings

Pathway 1

Listing 1: Hierarchical SFO path 1 fit with constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:32:35 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - k_cyan * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * k_cyan * cyan - k_JCZ38 * JCZ38
d_J9Z38/dt = + f_cyan_to_J9Z38 * k_cyan * cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 530.472 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
        cyan_0     log_k_cyan    log_k_JCZ38    log_k_J9Z38    log_k_JSE76
       95.3304        -3.8459        -3.1305        -5.0678        -5.3196
  f_cyan_ilr_1   f_cyan_ilr_2 f_JCZ38_qlogis
        0.8158        23.5335        11.8774

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_cyan log_k_JCZ38 log_k_J9Z38 log_k_JSE76
cyan_0          4.797     0.0000       0.000       0.000      0.0000
log_k_cyan      0.000     0.9619       0.000       0.000      0.0000
log_k_JCZ38     0.000     0.0000       2.139       0.000      0.0000
log_k_J9Z38     0.000     0.0000       0.000       1.639      0.0000
log_k_JSE76     0.000     0.0000       0.000       0.000      0.7894
f_cyan_ilr_1    0.000     0.0000       0.000       0.000      0.0000
f_cyan_ilr_2    0.000     0.0000       0.000       0.000      0.0000
f_JCZ38_qlogis  0.000     0.0000       0.000       0.000      0.0000
               f_cyan_ilr_1 f_cyan_ilr_2 f_JCZ38_qlogis
cyan_0               0.0000        0.000           0.00
log_k_cyan           0.0000        0.000           0.00
log_k_JCZ38          0.0000        0.000           0.00
log_k_J9Z38          0.0000        0.000           0.00
log_k_JSE76          0.0000        0.000           0.00
f_cyan_ilr_1         0.7714        0.000           0.00
f_cyan_ilr_2         0.0000        9.247           0.00
f_JCZ38_qlogis       0.0000        0.000          16.61

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2693 2687  -1331

Optimised parameters:
                     est.      lower      upper
cyan_0            95.1279  9.354e+01  9.671e+01
log_k_cyan        -3.8527 -4.367e+00 -3.338e+00
log_k_JCZ38       -3.0381 -4.187e+00 -1.889e+00
log_k_J9Z38       -5.0095 -5.623e+00 -4.396e+00
log_k_JSE76       -5.3357 -6.025e+00 -4.646e+00
f_cyan_ilr_1       0.8050  5.174e-01  1.093e+00
f_cyan_ilr_2      12.4820 -1.050e+06  1.051e+06
f_JCZ38_qlogis     1.2912  3.561e-01  2.226e+00
a.1                4.8393         NA         NA
SD.log_k_cyan      0.5840         NA         NA
SD.log_k_JCZ38     1.2740         NA         NA
SD.log_k_J9Z38     0.3172         NA         NA
SD.log_k_JSE76     0.5677         NA         NA
SD.f_cyan_ilr_1    0.2623         NA         NA
```

```
SD.f_cyan_ilr_2    1.3724         NA         NA
SD.f_JCZ38_qlogis  0.1464         NA         NA

Correlation is not available

Random effects:
                    est. lower upper
SD.log_k_cyan     0.5840    NA    NA
SD.log_k_JCZ38    1.2740    NA    NA
SD.log_k_J9Z38    0.3172    NA    NA
SD.log_k_JSE76    0.5677    NA    NA
SD.f_cyan_ilr_1   0.2623    NA    NA
SD.f_cyan_ilr_2   1.3724    NA    NA
SD.f_JCZ38_qlogis 0.1464    NA    NA

Variance model:
     est. lower upper
a.1 4.839    NA    NA

Backtransformed parameters:
                      est.     lower     upper
cyan_0           95.127935 93.542456 96.713413
k_cyan            0.021221  0.012687  0.035497
k_JCZ38           0.047924  0.015189  0.151213
k_J9Z38           0.006674  0.003612  0.012332
k_JSE76           0.004817  0.002417  0.009601
f_cyan_to_JCZ38   0.757402        NA        NA
f_cyan_to_J9Z38   0.242597        NA        NA
f_JCZ38_to_JSE76  0.784347  0.588098  0.902582

Resulting formation fractions:
                   ff
cyan_JCZ38  7.574e-01
cyan_J9Z38  2.426e-01
cyan_sink   9.839e-08
JCZ38_JSE76 7.843e-01
JCZ38_sink  2.157e-01

Estimated disappearance times:
        DT50   DT90
cyan   32.66 108.50
JCZ38  14.46  48.05
J9Z38 103.86 345.00
JSE76 143.91 478.04
```

Listing 2: Hierarchical SFO path 1 fit with two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:31:56 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - k_cyan * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * k_cyan * cyan - k_JCZ38 * JCZ38
d_J9Z38/dt = + f_cyan_to_J9Z38 * k_cyan * cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 491.09 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
        cyan_0     log_k_cyan    log_k_JCZ38    log_k_J9Z38    log_k_JSE76
       96.0039        -3.8907        -3.1276        -5.0069        -4.9367
  f_cyan_ilr_1   f_cyan_ilr_2 f_JCZ38_qlogis
        0.7937        22.3422        17.8932

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_cyan log_k_JCZ38 log_k_J9Z38 log_k_JSE76
cyan_0          4.859      0.000        0.00        0.00      0.0000
log_k_cyan      0.000      0.962        0.00        0.00      0.0000
log_k_JCZ38     0.000      0.000        2.04        0.00      0.0000
log_k_J9Z38     0.000      0.000        0.00        1.72      0.0000
log_k_JSE76     0.000      0.000        0.00        0.00      0.9076
f_cyan_ilr_1    0.000      0.000        0.00        0.00      0.0000
f_cyan_ilr_2    0.000      0.000        0.00        0.00      0.0000
f_JCZ38_qlogis  0.000      0.000        0.00        0.00      0.0000
               f_cyan_ilr_1 f_cyan_ilr_2 f_JCZ38_qlogis
cyan_0               0.0000        0.000           0.00
log_k_cyan           0.0000        0.000           0.00
log_k_JCZ38          0.0000        0.000           0.00
log_k_J9Z38          0.0000        0.000           0.00
log_k_JSE76          0.0000        0.000           0.00
f_cyan_ilr_1         0.7598        0.000           0.00
f_cyan_ilr_2         0.0000        8.939           0.00
f_JCZ38_qlogis       0.0000        0.000          14.49

Starting values for error model parameters:
a.1 b.1
  1   1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2658 2651  -1312

Optimised parameters:
                      est. lower upper
cyan_0            94.81681    NA    NA
log_k_cyan        -3.91558    NA    NA
log_k_JCZ38       -3.12715    NA    NA
log_k_J9Z38       -5.04840    NA    NA
log_k_JSE76       -5.10443    NA    NA
f_cyan_ilr_1       0.80760    NA    NA
f_cyan_ilr_2      48.66960    NA    NA
f_JCZ38_qlogis     3.03397    NA    NA
a.1                3.93879    NA    NA
b.1                0.08057    NA    NA
SD.log_k_cyan      0.58921    NA    NA
SD.log_k_JCZ38     1.29813    NA    NA
SD.log_k_J9Z38     0.68372    NA    NA
SD.log_k_JSE76     0.35128    NA    NA
SD.f_cyan_ilr_1    0.38352    NA    NA
SD.f_cyan_ilr_2    4.98884    NA    NA
SD.f_JCZ38_qlogis  1.75636    NA    NA

Correlation is not available
```

```
Random effects:
                     est. lower upper
SD.log_k_cyan     0.5892    NA    NA
SD.log_k_JCZ38    1.2981    NA    NA
SD.log_k_J9Z38    0.6837    NA    NA
SD.log_k_JSE76    0.3513    NA    NA
SD.f_cyan_ilr_1   0.3835    NA    NA
SD.f_cyan_ilr_2   4.9888    NA    NA
SD.f_JCZ38_qlogis 1.7564    NA    NA

Variance model:
       est. lower upper
a.1 3.93879    NA    NA
b.1 0.08057    NA    NA

Backtransformed parameters:
                      est. lower upper
cyan_0            94.81681    NA    NA
k_cyan             0.01993    NA    NA
k_JCZ38            0.04384    NA    NA
k_J9Z38            0.00642    NA    NA
k_JSE76            0.00607    NA    NA
f_cyan_to_JCZ38    0.75807    NA    NA
f_cyan_to_J9Z38    0.24193    NA    NA
f_JCZ38_to_JSE76   0.95409    NA    NA

Resulting formation fractions:
                ff
cyan_JCZ38  0.75807
cyan_J9Z38  0.24193
cyan_sink   0.00000
JCZ38_JSE76 0.95409
JCZ38_sink  0.04591

Estimated disappearance times:
        DT50   DT90
cyan   34.78 115.54
JCZ38  15.81  52.52
J9Z38 107.97 358.68
JSE76 114.20 379.35
```

Listing 3: Hierarchical FOMC path 1 fit with constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:34:08 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - (alpha/beta) * 1/((time/beta) + 1) * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * (alpha/beta) * 1/((time/beta) + 1) *
           cyan - k_JCZ38 * JCZ38
d_J9Z38/dt = + f_cyan_to_J9Z38 * (alpha/beta) * 1/((time/beta) + 1) *
           cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 623.314 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
        cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
      101.2314        -3.3680        -5.1108        -5.9416         0.7144
  f_cyan_ilr_2 f_JCZ38_qlogis      log_alpha       log_beta
        7.0229        14.9234        -0.1791         2.9811

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          5.416       0.000         0.0       0.000       0.0000
log_k_JCZ38     0.000       2.439         0.0       0.000       0.0000
log_k_J9Z38     0.000       0.000         1.7       0.000       0.0000
log_k_JSE76     0.000       0.000         0.0       1.856       0.0000
f_cyan_ilr_1    0.000       0.000         0.0       0.000       0.7164
f_cyan_ilr_2    0.000       0.000         0.0       0.000       0.0000
f_JCZ38_qlogis  0.000       0.000         0.0       0.000       0.0000
log_alpha       0.000       0.000         0.0       0.000       0.0000
log_beta        0.000       0.000         0.0       0.000       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis log_alpha log_beta
cyan_0                 0.00           0.00    0.0000   0.0000
log_k_JCZ38            0.00           0.00    0.0000   0.0000
log_k_J9Z38            0.00           0.00    0.0000   0.0000
log_k_JSE76            0.00           0.00    0.0000   0.0000
f_cyan_ilr_1           0.00           0.00    0.0000   0.0000
f_cyan_ilr_2          11.57           0.00    0.0000   0.0000
f_JCZ38_qlogis         0.00          18.81    0.0000   0.0000
log_alpha              0.00           0.00    0.4144   0.0000
log_beta               0.00           0.00    0.0000   0.5077

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2428 2421  -1196

Optimised parameters:
                    est.    lower    upper
cyan_0           101.1664 98.51265 103.8202
log_k_JCZ38       -3.3883 -4.78250  -1.9941
log_k_J9Z38       -5.3087 -5.91564  -4.7017
log_k_JSE76       -6.1313 -7.30061  -4.9619
f_cyan_ilr_1       0.7456  0.43782   1.0534
f_cyan_ilr_2       0.8181  0.24956   1.3866
f_JCZ38_qlogis     2.0467  0.61165   3.4817
log_alpha         -0.2391 -0.62806   0.1499
log_beta           2.8739  2.67664   3.0711
a.1                3.4160  3.17960   3.6525
SD.cyan_0          2.4355  0.40399   4.4671
SD.log_k_JCZ38     1.5654  0.57311   2.5576
SD.log_k_J9Z38     0.4645 -0.06533   0.9943
SD.log_k_JSE76     0.9841  0.10738   1.8609
SD.f_cyan_ilr_1    0.3285  0.10546   0.5515
```

```
SD.f_cyan_ilr_2     0.2276 -0.38711   0.8424
SD.f_JCZ38_qlogis   0.8340 -0.20970   1.8777
SD.log_alpha        0.4250  0.16017   0.6898

Correlation:
               cyan_0  l__JCZ3 l__J9Z3 l__JSE7 f_cy__1 f_cy__2 f_JCZ38 log_lph
log_k_JCZ38    -0.0159
log_k_J9Z38    -0.0546  0.0080
log_k_JSE76    -0.0337  0.0016  0.0074
f_cyan_ilr_1   -0.0095  0.0194 -0.1573  0.0003
f_cyan_ilr_2   -0.2733  0.0799  0.3059  0.0263  0.0125
f_JCZ38_qlogis  0.0755 -0.0783 -0.0516  0.1222 -0.1155 -0.5231
log_alpha      -0.0567  0.0120  0.0351  0.0189  0.0040  0.0829 -0.0502
log_beta       -0.2980  0.0461  0.1382  0.0758  0.0209  0.4079 -0.2053  0.2759

Random effects:
                     est.    lower  upper
SD.cyan_0         2.4355  0.40399 4.4671
SD.log_k_JCZ38    1.5654  0.57311 2.5576
SD.log_k_J9Z38    0.4645 -0.06533 0.9943
SD.log_k_JSE76    0.9841  0.10738 1.8609
SD.f_cyan_ilr_1   0.3285  0.10546 0.5515
SD.f_cyan_ilr_2   0.2276 -0.38711 0.8424
SD.f_JCZ38_qlogis 0.8340 -0.20970 1.8777
SD.log_alpha      0.4250  0.16017 0.6898

Variance model:
     est. lower upper
a.1 3.416  3.18 3.652

Backtransformed parameters:
                       est.     lower     upper
cyan_0           1.012e+02 9.851e+01 103.82023
k_JCZ38          3.377e-02 8.375e-03   0.13614
k_J9Z38          4.948e-03 2.697e-03   0.00908
k_JSE76          2.174e-03 6.751e-04   0.00700
f_cyan_to_JCZ38  6.389e-01        NA        NA
f_cyan_to_J9Z38  2.226e-01        NA        NA
f_JCZ38_to_JSE76 8.856e-01 6.483e-01   0.97016
alpha            7.873e-01 5.336e-01   1.16166
beta             1.771e+01 1.454e+01  21.56509

Resulting formation fractions:
                ff
cyan_JCZ38  0.6389
cyan_J9Z38  0.2226
cyan_sink   0.1385
JCZ38_JSE76 0.8856
JCZ38_sink  0.1144

Estimated disappearance times:
        DT50    DT90 DT50back
cyan   25.00  312.06    93.94
JCZ38  20.53   68.19       NA
J9Z38 140.07  465.32       NA
JSE76 318.86 1059.22       NA
```

Listing 4: Hierarchical FOMC path 1 fit with two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:32:56 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - (alpha/beta) * 1/((time/beta) + 1) * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * (alpha/beta) * 1/((time/beta) + 1) *
           cyan - k_JCZ38 * JCZ38
d_J9Z38/dt = + f_cyan_to_J9Z38 * (alpha/beta) * 1/((time/beta) + 1) *
           cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 550.58 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
        cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
     101.13294       -3.32499       -5.09097       -5.93566        0.71359
  f_cyan_ilr_2 f_JCZ38_qlogis      log_alpha       log_beta
      10.30315       14.62272       -0.09633        3.10634

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          5.649       0.000        0.00        0.00       0.0000
log_k_JCZ38     0.000       2.319        0.00        0.00       0.0000
log_k_J9Z38     0.000       0.000        1.73        0.00       0.0000
log_k_JSE76     0.000       0.000        0.00        1.86       0.0000
f_cyan_ilr_1    0.000       0.000        0.00        0.00       0.7183
f_cyan_ilr_2    0.000       0.000        0.00        0.00       0.0000
f_JCZ38_qlogis  0.000       0.000        0.00        0.00       0.0000
log_alpha       0.000       0.000        0.00        0.00       0.0000
log_beta        0.000       0.000        0.00        0.00       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis log_alpha log_beta
cyan_0                 0.00           0.00    0.0000   0.0000
log_k_JCZ38            0.00           0.00    0.0000   0.0000
log_k_J9Z38            0.00           0.00    0.0000   0.0000
log_k_JSE76            0.00           0.00    0.0000   0.0000
f_cyan_ilr_1           0.00           0.00    0.0000   0.0000
f_cyan_ilr_2          12.85           0.00    0.0000   0.0000
f_JCZ38_qlogis         0.00          18.54    0.0000   0.0000
log_alpha              0.00           0.00    0.3142   0.0000
log_beta               0.00           0.00    0.0000   0.7333

Starting values for error model parameters:
a.1 b.1
  1   1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2424 2416  -1193

Optimised parameters:
                     est. lower upper
cyan_0            100.65667    NA    NA
log_k_JCZ38        -3.45782    NA    NA
log_k_J9Z38        -5.23476    NA    NA
log_k_JSE76        -5.71827    NA    NA
f_cyan_ilr_1        0.68389    NA    NA
f_cyan_ilr_2        0.61027    NA    NA
f_JCZ38_qlogis    116.27482    NA    NA
log_alpha          -0.14484    NA    NA
log_beta            3.03220    NA    NA
a.1                 3.11051    NA    NA
b.1                 0.04508    NA    NA
SD.log_k_JCZ38      1.39961    NA    NA
SD.log_k_J9Z38      0.57920    NA    NA
SD.log_k_JSE76      0.68364    NA    NA
SD.f_cyan_ilr_1     0.31477    NA    NA
```

```
SD.f_cyan_ilr_2     0.37716    NA    NA
SD.f_JCZ38_qlogis   5.52695    NA    NA
SD.log_alpha        0.22823    NA    NA
SD.log_beta         0.39161    NA    NA

Correlation is not available

Random effects:
                     est. lower upper
SD.log_k_JCZ38    1.3996    NA    NA
SD.log_k_J9Z38    0.5792    NA    NA
SD.log_k_JSE76    0.6836    NA    NA
SD.f_cyan_ilr_1   0.3148    NA    NA
SD.f_cyan_ilr_2   0.3772    NA    NA
SD.f_JCZ38_qlogis 5.5270    NA    NA
SD.log_alpha      0.2282    NA    NA
SD.log_beta       0.3916    NA    NA

Variance model:
       est. lower upper
a.1 3.11051    NA    NA
b.1 0.04508    NA    NA

Backtransformed parameters:
                      est. lower upper
cyan_0           1.007e+02    NA    NA
k_JCZ38          3.150e-02    NA    NA
k_J9Z38          5.328e-03    NA    NA
k_JSE76          3.285e-03    NA    NA
f_cyan_to_JCZ38  5.980e-01    NA    NA
f_cyan_to_J9Z38  2.273e-01    NA    NA
f_JCZ38_to_JSE76 1.000e+00    NA    NA
alpha            8.652e-01    NA    NA
beta             2.074e+01    NA    NA

Resulting formation fractions:
                ff
cyan_JCZ38  0.5980
cyan_J9Z38  0.2273
cyan_sink   0.1746
JCZ38_JSE76 1.0000
JCZ38_sink  0.0000

Estimated disappearance times:
        DT50  DT90 DT50back
cyan   25.48 276.2    83.15
JCZ38  22.01  73.1       NA
J9Z38 130.09 432.2       NA
JSE76 210.98 700.9       NA
```

Listing 5: Hierarchical DFOP path 1 fit with constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:33:28 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
           time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
           * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
           g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
           exp(-k2 * time))) * cyan - k_JCZ38 * JCZ38
d_J9Z38/dt = + f_cyan_to_J9Z38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
           g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
           exp(-k2 * time))) * cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 583.053 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
       cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
     102.0643        -3.4008        -5.0024        -5.8612         0.6855
  f_cyan_ilr_2 f_JCZ38_qlogis         log_k1         log_k2       g_qlogis
       1.2366        13.6901        -1.8641        -4.5063        -0.6468

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          4.466       0.000       0.000       0.000       0.0000
log_k_JCZ38     0.000       2.382       0.000       0.000       0.0000
log_k_J9Z38     0.000       0.000       1.595       0.000       0.0000
log_k_JSE76     0.000       0.000       0.000       1.245       0.0000
f_cyan_ilr_1    0.000       0.000       0.000       0.000       0.6852
f_cyan_ilr_2    0.000       0.000       0.000       0.000       0.0000
f_JCZ38_qlogis  0.000       0.000       0.000       0.000       0.0000
log_k1          0.000       0.000       0.000       0.000       0.0000
log_k2          0.000       0.000       0.000       0.000       0.0000
g_qlogis        0.000       0.000       0.000       0.000       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis log_k1 log_k2 g_qlogis
cyan_0                0.00           0.00 0.0000 0.0000    0.000
log_k_JCZ38           0.00           0.00 0.0000 0.0000    0.000
log_k_J9Z38           0.00           0.00 0.0000 0.0000    0.000
log_k_JSE76           0.00           0.00 0.0000 0.0000    0.000
f_cyan_ilr_1          0.00           0.00 0.0000 0.0000    0.000
f_cyan_ilr_2          1.28           0.00 0.0000 0.0000    0.000
f_JCZ38_qlogis        0.00          16.08 0.0000 0.0000    0.000
log_k1                0.00           0.00 0.9866 0.0000    0.000
log_k2                0.00           0.00 0.0000 0.5953    0.000
g_qlogis              0.00           0.00 0.0000 0.0000    1.583

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2403 2395  -1182

Optimised parameters:
                    est. lower upper
cyan_0            102.5565    NA    NA
log_k_JCZ38        -3.4729    NA    NA
log_k_J9Z38        -5.1533    NA    NA
log_k_JSE76        -5.6669    NA    NA
f_cyan_ilr_1        0.6665    NA    NA
f_cyan_ilr_2        0.5191    NA    NA
f_JCZ38_qlogis     37.0113    NA    NA
log_k1             -1.8497    NA    NA
log_k2             -4.4931    NA    NA
```

```
g_qlogis           -0.6383    NA    NA
a.1                 3.2397    NA    NA
SD.log_k_JCZ38      1.4286    NA    NA
SD.log_k_J9Z38      0.5312    NA    NA
SD.log_k_JSE76      0.6627    NA    NA
SD.f_cyan_ilr_1     0.3013    NA    NA
SD.f_cyan_ilr_2     0.2980    NA    NA
SD.f_JCZ38_qlogis   0.1637    NA    NA
SD.log_k1           0.5069    NA    NA
SD.log_k2           0.3828    NA    NA
SD.g_qlogis         0.8641    NA    NA

Correlation is not available

Random effects:
                    est. lower upper
SD.log_k_JCZ38    1.4286    NA    NA
SD.log_k_J9Z38    0.5312    NA    NA
SD.log_k_JSE76    0.6627    NA    NA
SD.f_cyan_ilr_1   0.3013    NA    NA
SD.f_cyan_ilr_2   0.2980    NA    NA
SD.f_JCZ38_qlogis 0.1637    NA    NA
SD.log_k1         0.5069    NA    NA
SD.log_k2         0.3828    NA    NA
SD.g_qlogis       0.8641    NA    NA

Variance model:
    est. lower upper
a.1 3.24    NA    NA

Backtransformed parameters:
                       est. lower upper
cyan_0           1.026e+02    NA    NA
k_JCZ38          3.103e-02    NA    NA
k_J9Z38          5.780e-03    NA    NA
k_JSE76          3.459e-03    NA    NA
f_cyan_to_JCZ38  5.813e-01    NA    NA
f_cyan_to_J9Z38  2.265e-01    NA    NA
f_JCZ38_to_JSE76 1.000e+00    NA    NA
k1               1.573e-01    NA    NA
k2               1.119e-02    NA    NA
g                3.456e-01    NA    NA

Resulting formation fractions:
                ff
cyan_JCZ38  0.5813
cyan_J9Z38  0.2265
cyan_sink   0.1922
JCZ38_JSE76 1.0000
JCZ38_sink  0.0000

Estimated disappearance times:
        DT50   DT90 DT50back DT50_k1 DT50_k2
cyan   25.23 167.94    50.55   4.407   61.97
JCZ38  22.34  74.22       NA      NA      NA
J9Z38 119.92 398.36       NA      NA      NA
JSE76 200.41 665.76       NA      NA      NA
```

Listing 6: Hierarchical DFOP path 1 fit with two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:37:24 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
           time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
           * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
           g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
           exp(-k2 * time))) * cyan - k_JCZ38 * JCZ38
d_J9Z38/dt = + f_cyan_to_J9Z38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
           g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
           exp(-k2 * time))) * cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 818.805 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
       cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
     101.3964        -3.3626        -4.9792        -5.8727         0.6814
  f_cyan_ilr_2 f_JCZ38_qlogis         log_k1         log_k2       g_qlogis
       6.8713        13.6901        -1.9222        -4.5035        -0.7172

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          5.317       0.000       0.000       0.000       0.0000
log_k_JCZ38     0.000       2.272       0.000       0.000       0.0000
log_k_J9Z38     0.000       0.000       1.633       0.000       0.0000
log_k_JSE76     0.000       0.000       0.000       1.271       0.0000
f_cyan_ilr_1    0.000       0.000       0.000       0.000       0.6839
f_cyan_ilr_2    0.000       0.000       0.000       0.000       0.0000
f_JCZ38_qlogis  0.000       0.000       0.000       0.000       0.0000
log_k1          0.000       0.000       0.000       0.000       0.0000
log_k2          0.000       0.000       0.000       0.000       0.0000
g_qlogis        0.000       0.000       0.000       0.000       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis log_k1 log_k2 g_qlogis
cyan_0                 0.00           0.00 0.0000 0.0000    0.000
log_k_JCZ38            0.00           0.00 0.0000 0.0000    0.000
log_k_J9Z38            0.00           0.00 0.0000 0.0000    0.000
log_k_JSE76            0.00           0.00 0.0000 0.0000    0.000
f_cyan_ilr_1           0.00           0.00 0.0000 0.0000    0.000
f_cyan_ilr_2          11.95           0.00 0.0000 0.0000    0.000
f_JCZ38_qlogis         0.00          16.08 0.0000 0.0000    0.000
log_k1                 0.00           0.00 0.9496 0.0000    0.000
log_k2                 0.00           0.00 0.0000 0.5846    0.000
g_qlogis               0.00           0.00 0.0000 0.0000    1.719

Starting values for error model parameters:
a.1 b.1
  1   1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2398 2390  -1179

Optimised parameters:
                      est. lower upper
cyan_0            100.69709    NA    NA
log_k_JCZ38        -3.46669    NA    NA
log_k_J9Z38        -5.05076    NA    NA
log_k_JSE76        -5.55558    NA    NA
f_cyan_ilr_1        0.66045    NA    NA
f_cyan_ilr_2        0.84275    NA    NA
f_JCZ38_qlogis     64.22404    NA    NA
log_k1             -2.17715    NA    NA
log_k2             -4.55002    NA    NA
```

```
g_qlogis           -0.55920    NA    NA
a.1                 2.95785    NA    NA
b.1                 0.04456    NA    NA
SD.log_k_JCZ38      1.39881    NA    NA
SD.log_k_J9Z38      0.67788    NA    NA
SD.log_k_JSE76      0.52603    NA    NA
SD.f_cyan_ilr_1     0.32490    NA    NA
SD.f_cyan_ilr_2     0.53923    NA    NA
SD.f_JCZ38_qlogis   2.75576    NA    NA
SD.log_k2           0.30694    NA    NA
SD.g_qlogis         0.83619    NA    NA

Correlation is not available

Random effects:
                    est. lower upper
SD.log_k_JCZ38    1.3988    NA    NA
SD.log_k_J9Z38    0.6779    NA    NA
SD.log_k_JSE76    0.5260    NA    NA
SD.f_cyan_ilr_1   0.3249    NA    NA
SD.f_cyan_ilr_2   0.5392    NA    NA
SD.f_JCZ38_qlogis 2.7558    NA    NA
SD.log_k2         0.3069    NA    NA
SD.g_qlogis       0.8362    NA    NA

Variance model:
       est. lower upper
a.1 2.95785    NA    NA
b.1 0.04456    NA    NA

Backtransformed parameters:
                       est. lower upper
cyan_0           1.007e+02    NA    NA
k_JCZ38          3.122e-02    NA    NA
k_J9Z38          6.404e-03    NA    NA
k_JSE76          3.866e-03    NA    NA
f_cyan_to_JCZ38  6.187e-01    NA    NA
f_cyan_to_J9Z38  2.431e-01    NA    NA
f_JCZ38_to_JSE76 1.000e+00    NA    NA
k1               1.134e-01    NA    NA
k2               1.057e-02    NA    NA
g                3.637e-01    NA    NA

Resulting formation fractions:
                ff
cyan_JCZ38  0.6187
cyan_J9Z38  0.2431
cyan_sink   0.1382
JCZ38_JSE76 1.0000
JCZ38_sink  0.0000

Estimated disappearance times:
        DT50   DT90 DT50back DT50_k1 DT50_k2
cyan   26.35 175.12    52.72   6.114    65.6
JCZ38  22.20  73.75       NA      NA      NA
J9Z38 108.23 359.53       NA      NA      NA
JSE76 179.30 595.62       NA      NA      NA
```

Listing 7: Hierarchical SFORB path 1 fit with constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:32:56 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan_free/dt = - k_cyan_free * cyan_free - k_cyan_free_bound *
          cyan_free + k_cyan_bound_free * cyan_bound
d_cyan_bound/dt = + k_cyan_free_bound * cyan_free - k_cyan_bound_free *
          cyan_bound
d_JCZ38/dt = + f_cyan_free_to_JCZ38 * k_cyan_free * cyan_free - k_JCZ38
          * JCZ38
d_J9Z38/dt = + f_cyan_free_to_J9Z38 * k_cyan_free * cyan_free - k_J9Z38
          * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 551.176 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
          cyan_free_0       log_k_cyan_free log_k_cyan_free_bound
            102.0643               -2.8987               -2.7077
log_k_cyan_bound_free           log_k_JCZ38           log_k_J9Z38
              -3.4717               -3.4008               -5.0024
          log_k_JSE76          f_cyan_ilr_1          f_cyan_ilr_2
              -5.8613                0.6855                1.2366
       f_JCZ38_qlogis
              13.7395

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                     cyan_free_0 log_k_cyan_free log_k_cyan_free_bound
cyan_free_0                4.466          0.0000                 0.000
log_k_cyan_free            0.000          0.6158                 0.000
log_k_cyan_free_bound      0.000          0.0000                 1.463
log_k_cyan_bound_free      0.000          0.0000                 0.000
log_k_JCZ38                0.000          0.0000                 0.000
log_k_J9Z38                0.000          0.0000                 0.000
log_k_JSE76                0.000          0.0000                 0.000
f_cyan_ilr_1               0.000          0.0000                 0.000
f_cyan_ilr_2               0.000          0.0000                 0.000
f_JCZ38_qlogis             0.000          0.0000                 0.000
                     log_k_cyan_bound_free log_k_JCZ38 log_k_J9Z38 log_k_JSE76
cyan_free_0                          0.000       0.000       0.000       0.000
log_k_cyan_free                      0.000       0.000       0.000       0.000
log_k_cyan_free_bound                0.000       0.000       0.000       0.000
log_k_cyan_bound_free                1.058       0.000       0.000       0.000
log_k_JCZ38                          0.000       2.382       0.000       0.000
log_k_J9Z38                          0.000       0.000       1.595       0.000
log_k_JSE76                          0.000       0.000       0.000       1.245
f_cyan_ilr_1                         0.000       0.000       0.000       0.000
f_cyan_ilr_2                         0.000       0.000       0.000       0.000
f_JCZ38_qlogis                       0.000       0.000       0.000       0.000
                     f_cyan_ilr_1 f_cyan_ilr_2 f_JCZ38_qlogis
cyan_free_0                0.0000         0.00           0.00
log_k_cyan_free            0.0000         0.00           0.00
log_k_cyan_free_bound      0.0000         0.00           0.00
log_k_cyan_bound_free      0.0000         0.00           0.00
log_k_JCZ38                0.0000         0.00           0.00
log_k_J9Z38                0.0000         0.00           0.00
log_k_JSE76                0.0000         0.00           0.00
f_cyan_ilr_1               0.6852         0.00           0.00
f_cyan_ilr_2               0.0000         1.28           0.00
f_JCZ38_qlogis             0.0000         0.00          16.13

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
```

```
   AIC  BIC logLik
  2401 2394  -1181

Optimised parameters:
                            est. lower upper
cyan_free_0              102.8136    NA    NA
log_k_cyan_free           -2.7935    NA    NA
log_k_cyan_free_bound     -2.5440    NA    NA
log_k_cyan_bound_free     -3.4303    NA    NA
log_k_JCZ38               -3.5010    NA    NA
log_k_J9Z38               -5.1226    NA    NA
log_k_JSE76               -5.6314    NA    NA
f_cyan_ilr_1               0.6609    NA    NA
f_cyan_ilr_2               0.5085    NA    NA
f_JCZ38_qlogis            44.0153    NA    NA
a.1                        3.2318    NA    NA
SD.log_k_cyan_free         0.3211    NA    NA
SD.log_k_cyan_free_bound   0.8408    NA    NA
SD.log_k_cyan_bound_free   0.5724    NA    NA
SD.log_k_JCZ38             1.4925    NA    NA
SD.log_k_J9Z38             0.5816    NA    NA
SD.log_k_JSE76             0.6037    NA    NA
SD.f_cyan_ilr_1            0.3115    NA    NA
SD.f_cyan_ilr_2            0.3436    NA    NA
SD.f_JCZ38_qlogis          4.8937    NA    NA

Correlation is not available

Random effects:
                           est. lower upper
SD.log_k_cyan_free       0.3211    NA    NA
SD.log_k_cyan_free_bound 0.8408    NA    NA
SD.log_k_cyan_bound_free 0.5724    NA    NA
SD.log_k_JCZ38           1.4925    NA    NA
SD.log_k_J9Z38           0.5816    NA    NA
SD.log_k_JSE76           0.6037    NA    NA
SD.f_cyan_ilr_1          0.3115    NA    NA
SD.f_cyan_ilr_2          0.3436    NA    NA
SD.f_JCZ38_qlogis        4.8937    NA    NA

Variance model:
     est. lower upper
a.1 3.232    NA    NA

Backtransformed parameters:
                             est. lower upper
cyan_free_0           1.028e+02    NA    NA
k_cyan_free           6.120e-02    NA    NA
k_cyan_free_bound     7.855e-02    NA    NA
k_cyan_bound_free     3.238e-02    NA    NA
k_JCZ38               3.017e-02    NA    NA
k_J9Z38               5.961e-03    NA    NA
k_JSE76               3.584e-03    NA    NA
f_cyan_free_to_JCZ38 5.784e-01    NA    NA
f_cyan_free_to_J9Z38 2.271e-01    NA    NA
f_JCZ38_to_JSE76     1.000e+00    NA    NA

Estimated Eigenvalues of SFORB model(s):
cyan_b1 cyan_b2  cyan_g
0.15973 0.01241 0.33124

Resulting formation fractions:
                    ff
cyan_free_JCZ38 0.5784
cyan_free_J9Z38 0.2271
cyan_free_sink  0.1945
cyan_free       1.0000
JCZ38_JSE76     1.0000
JCZ38_sink      0.0000

Estimated disappearance times:
        DT50   DT90 DT50back DT50_cyan_b1 DT50_cyan_b2
cyan   24.51 153.18    46.11         4.34        55.87
JCZ38  22.98  76.33       NA           NA           NA
J9Z38 116.28 386.29       NA           NA           NA
JSE76 193.42 642.53       NA           NA           NA
```

Listing 8: Hierarchical SFORB path 1 fit with two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:36:44 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan_free/dt = - k_cyan_free * cyan_free - k_cyan_free_bound *
          cyan_free + k_cyan_bound_free * cyan_bound
d_cyan_bound/dt = + k_cyan_free_bound * cyan_free - k_cyan_bound_free *
          cyan_bound
d_JCZ38/dt = + f_cyan_free_to_JCZ38 * k_cyan_free * cyan_free - k_JCZ38
          * JCZ38
d_J9Z38/dt = + f_cyan_free_to_J9Z38 * k_cyan_free * cyan_free - k_J9Z38
          * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 778.828 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
          cyan_free_0       log_k_cyan_free log_k_cyan_free_bound
             101.3964               -2.9881               -2.7949
log_k_cyan_bound_free           log_k_JCZ38           log_k_J9Z38
              -3.4376               -3.3626               -4.9792
          log_k_JSE76          f_cyan_ilr_1          f_cyan_ilr_2
              -5.8727                0.6814                6.7399
       f_JCZ38_qlogis
              13.7395

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                     cyan_free_0 log_k_cyan_free log_k_cyan_free_bound
cyan_free_0                5.317          0.0000                 0.000
log_k_cyan_free            0.000          0.7301                 0.000
log_k_cyan_free_bound      0.000          0.0000                 1.384
log_k_cyan_bound_free      0.000          0.0000                 0.000
log_k_JCZ38                0.000          0.0000                 0.000
log_k_J9Z38                0.000          0.0000                 0.000
log_k_JSE76                0.000          0.0000                 0.000
f_cyan_ilr_1               0.000          0.0000                 0.000
f_cyan_ilr_2               0.000          0.0000                 0.000
f_JCZ38_qlogis             0.000          0.0000                 0.000
                     log_k_cyan_bound_free log_k_JCZ38 log_k_J9Z38 log_k_JSE76
cyan_free_0                          0.000       0.000       0.000       0.000
log_k_cyan_free                      0.000       0.000       0.000       0.000
log_k_cyan_free_bound                0.000       0.000       0.000       0.000
log_k_cyan_bound_free                1.109       0.000       0.000       0.000
log_k_JCZ38                          0.000       2.272       0.000       0.000
log_k_J9Z38                          0.000       0.000       1.633       0.000
log_k_JSE76                          0.000       0.000       0.000       1.271
f_cyan_ilr_1                         0.000       0.000       0.000       0.000
f_cyan_ilr_2                         0.000       0.000       0.000       0.000
f_JCZ38_qlogis                       0.000       0.000       0.000       0.000
                     f_cyan_ilr_1 f_cyan_ilr_2 f_JCZ38_qlogis
cyan_free_0                0.0000         0.00           0.00
log_k_cyan_free            0.0000         0.00           0.00
log_k_cyan_free_bound      0.0000         0.00           0.00
log_k_cyan_bound_free      0.0000         0.00           0.00
log_k_JCZ38                0.0000         0.00           0.00
log_k_J9Z38                0.0000         0.00           0.00
log_k_JSE76                0.0000         0.00           0.00
f_cyan_ilr_1               0.6838         0.00           0.00
f_cyan_ilr_2               0.0000        11.69           0.00
f_JCZ38_qlogis             0.0000         0.00          16.13

Starting values for error model parameters:
a.1 b.1
  1   1

Results:

Likelihood computed by importance sampling
```

```
   AIC  BIC logLik
  2400 2392  -1180

Optimised parameters:
                             est. lower upper
cyan_free_0              100.56004    NA    NA
log_k_cyan_free           -3.12657    NA    NA
log_k_cyan_free_bound     -3.16825    NA    NA
log_k_cyan_bound_free     -3.66003    NA    NA
log_k_JCZ38               -3.47278    NA    NA
log_k_J9Z38               -5.06823    NA    NA
log_k_JSE76               -5.54327    NA    NA
f_cyan_ilr_1               0.66631    NA    NA
f_cyan_ilr_2               0.82898    NA    NA
f_JCZ38_qlogis            38.31115    NA    NA
a.1                        2.98352    NA    NA
b.1                        0.04388    NA    NA
SD.log_k_cyan_free         0.49145    NA    NA
SD.log_k_cyan_bound_free   0.27347    NA    NA
SD.log_k_JCZ38             1.41193    NA    NA
SD.log_k_J9Z38             0.66073    NA    NA
SD.log_k_JSE76             0.55885    NA    NA
SD.f_cyan_ilr_1            0.33020    NA    NA
SD.f_cyan_ilr_2            0.51367    NA    NA
SD.f_JCZ38_qlogis          5.52122    NA    NA

Correlation is not available

Random effects:
                           est. lower upper
SD.log_k_cyan_free       0.4914    NA    NA
SD.log_k_cyan_bound_free 0.2735    NA    NA
SD.log_k_JCZ38           1.4119    NA    NA
SD.log_k_J9Z38           0.6607    NA    NA
SD.log_k_JSE76           0.5589    NA    NA
SD.f_cyan_ilr_1          0.3302    NA    NA
SD.f_cyan_ilr_2          0.5137    NA    NA
SD.f_JCZ38_qlogis        5.5212    NA    NA

Variance model:
       est. lower upper
a.1 2.98352    NA    NA
b.1 0.04388    NA    NA

Backtransformed parameters:
                            est. lower upper
cyan_free_0           1.006e+02    NA    NA
k_cyan_free           4.387e-02    NA    NA
k_cyan_free_bound     4.208e-02    NA    NA
k_cyan_bound_free     2.573e-02    NA    NA
k_JCZ38               3.103e-02    NA    NA
k_J9Z38               6.294e-03    NA    NA
k_JSE76               3.914e-03    NA    NA
f_cyan_free_to_JCZ38  6.188e-01    NA    NA
f_cyan_free_to_J9Z38  2.412e-01    NA    NA
f_JCZ38_to_JSE76      1.000e+00    NA    NA

Estimated Eigenvalues of SFORB model(s):
cyan_b1 cyan_b2  cyan_g
0.10044 0.01124 0.36580

Resulting formation fractions:
                    ff
cyan_free_JCZ38 0.6188
cyan_free_J9Z38 0.2412
cyan_free_sink  0.1400
cyan_free       1.0000
JCZ38_JSE76     1.0000
JCZ38_sink      0.0000

Estimated disappearance times:
        DT50  DT90 DT50back DT50_cyan_b1 DT50_cyan_b2
cyan   26.05 164.4    49.48        6.901        61.67
JCZ38  22.34  74.2       NA           NA           NA
J9Z38 110.14 365.9       NA           NA           NA
JSE76 177.11 588.3       NA           NA           NA
```

Listing 9: Hierarchical HS path 1 fit with constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:33:28 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - ifelse(time <= tb, k1, k2) * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * ifelse(time <= tb, k1, k2) * cyan -
           k_JCZ38 * JCZ38
d_J9Z38/dt = + f_cyan_to_J9Z38 * ifelse(time <= tb, k1, k2) * cyan -
           k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 583.355 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
        cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
      102.8845        -3.4495        -4.9355        -5.6040         0.6468
  f_cyan_ilr_2 f_JCZ38_qlogis         log_k1         log_k2         log_tb
        1.2396         9.7220        -2.9079        -4.1810         1.7813

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          5.406        0.00        0.00       0.000       0.0000
log_k_JCZ38     0.000        2.33        0.00       0.000       0.0000
log_k_J9Z38     0.000        0.00        1.59       0.000       0.0000
log_k_JSE76     0.000        0.00        0.00       1.013       0.0000
f_cyan_ilr_1    0.000        0.00        0.00       0.000       0.6367
f_cyan_ilr_2    0.000        0.00        0.00       0.000       0.0000
f_JCZ38_qlogis  0.000        0.00        0.00       0.000       0.0000
log_k1          0.000        0.00        0.00       0.000       0.0000
log_k2          0.000        0.00        0.00       0.000       0.0000
log_tb          0.000        0.00        0.00       0.000       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis log_k1 log_k2 log_tb
cyan_0                0.000           0.00 0.0000 0.0000 0.0000
log_k_JCZ38           0.000           0.00 0.0000 0.0000 0.0000
log_k_J9Z38           0.000           0.00 0.0000 0.0000 0.0000
log_k_JSE76           0.000           0.00 0.0000 0.0000 0.0000
f_cyan_ilr_1          0.000           0.00 0.0000 0.0000 0.0000
f_cyan_ilr_2          2.038           0.00 0.0000 0.0000 0.0000
f_JCZ38_qlogis        0.000          10.33 0.0000 0.0000 0.0000
log_k1                0.000           0.00 0.7006 0.0000 0.0000
log_k2                0.000           0.00 0.0000 0.8928 0.0000
log_tb                0.000           0.00 0.0000 0.0000 0.6773

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2427 2419  -1194

Optimised parameters:
                      est.      lower      upper
cyan_0            101.9660  1.005e+02  1.035e+02
log_k_JCZ38        -3.4698 -4.716e+00 -2.224e+00
log_k_J9Z38        -5.0947 -5.740e+00 -4.450e+00
log_k_JSE76        -5.5977 -6.321e+00 -4.875e+00
f_cyan_ilr_1        0.6595  3.734e-01  9.456e-01
f_cyan_ilr_2        0.5905  1.664e-01  1.015e+00
f_JCZ38_qlogis     25.8627 -4.224e+05  4.225e+05
log_k1             -3.0884 -3.453e+00 -2.723e+00
log_k2             -4.3877 -4.778e+00 -3.998e+00
log_tb              2.3057  1.715e+00  2.896e+00
a.1                 3.3228         NA         NA
SD.log_k_JCZ38      1.4071         NA         NA
SD.log_k_J9Z38      0.5774         NA         NA
```

```
SD.log_k_JSE76      0.6214         NA         NA
SD.f_cyan_ilr_1     0.3058         NA         NA
SD.f_cyan_ilr_2     0.3470         NA         NA
SD.f_JCZ38_qlogis   0.0644         NA         NA
SD.log_k1           0.3994         NA         NA
SD.log_k2           0.4373         NA         NA
SD.log_tb           0.6419         NA         NA

Correlation is not available

Random effects:
                     est. lower upper
SD.log_k_JCZ38    1.4071    NA    NA
SD.log_k_J9Z38    0.5774    NA    NA
SD.log_k_JSE76    0.6214    NA    NA
SD.f_cyan_ilr_1   0.3058    NA    NA
SD.f_cyan_ilr_2   0.3470    NA    NA
SD.f_JCZ38_qlogis 0.0644    NA    NA
SD.log_k1         0.3994    NA    NA
SD.log_k2         0.4373    NA    NA
SD.log_tb         0.6419    NA    NA

Variance model:
     est. lower upper
a.1 3.323    NA    NA

Backtransformed parameters:
                       est.     lower     upper
cyan_0           1.020e+02 1.005e+02 1.035e+02
k_JCZ38          3.112e-02 8.951e-03 1.082e-01
k_J9Z38          6.129e-03 3.216e-03 1.168e-02
k_JSE76          3.706e-03 1.798e-03 7.639e-03
f_cyan_to_JCZ38  5.890e-01        NA        NA
f_cyan_to_J9Z38  2.318e-01        NA        NA
f_JCZ38_to_JSE76 1.000e+00 0.000e+00 1.000e+00
k1               4.558e-02 3.164e-02 6.565e-02
k2               1.243e-02 8.417e-03 1.835e-02
tb               1.003e+01 5.557e+00 1.811e+01

Resulting formation fractions:
                  ff
cyan_JCZ38  5.890e-01
cyan_J9Z38  2.318e-01
cyan_sink   1.793e-01
JCZ38_JSE76 1.000e+00
JCZ38_sink  5.861e-12

Estimated disappearance times:
        DT50   DT90 DT50back DT50_k1 DT50_k2
cyan   29.02 158.51    47.72   15.21   55.77
JCZ38  22.27  73.98       NA      NA      NA
J9Z38 113.09 375.69       NA      NA      NA
JSE76 187.01 621.23       NA      NA      NA
```

Pathway 2

Listing 10: Hierarchical FOMC path 2 fit with two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:46:09 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - (alpha/beta) * 1/((time/beta) + 1) * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * (alpha/beta) * 1/((time/beta) + 1) *
           cyan - k_JCZ38 * JCZ38 + f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_to_J9Z38 * (alpha/beta) * 1/((time/beta) + 1) *
           cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 513.642 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
        cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
      102.4477        -1.8631        -5.1087        -2.5114         0.6826
  f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis      log_alpha       log_beta
        4.7944        15.9616        13.1566        -0.1564         2.9781

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          7.701       0.000       0.000       0.000       0.0000
log_k_JCZ38     0.000       1.448       0.000       0.000       0.0000
log_k_J9Z38     0.000       0.000       1.724       0.000       0.0000
log_k_JSE76     0.000       0.000       0.000       3.659       0.0000
f_cyan_ilr_1    0.000       0.000       0.000       0.000       0.6356
f_cyan_ilr_2    0.000       0.000       0.000       0.000       0.0000
f_JCZ38_qlogis  0.000       0.000       0.000       0.000       0.0000
f_JSE76_qlogis  0.000       0.000       0.000       0.000       0.0000
log_alpha       0.000       0.000       0.000       0.000       0.0000
log_beta        0.000       0.000       0.000       0.000       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis log_alpha log_beta
cyan_0                 0.00           0.00           0.00    0.0000   0.0000
log_k_JCZ38            0.00           0.00           0.00    0.0000   0.0000
log_k_J9Z38            0.00           0.00           0.00    0.0000   0.0000
log_k_JSE76            0.00           0.00           0.00    0.0000   0.0000
f_cyan_ilr_1           0.00           0.00           0.00    0.0000   0.0000
f_cyan_ilr_2          10.32           0.00           0.00    0.0000   0.0000
f_JCZ38_qlogis         0.00          12.23           0.00    0.0000   0.0000
f_JSE76_qlogis         0.00           0.00          14.99    0.0000   0.0000
log_alpha              0.00           0.00           0.00    0.3924   0.0000
log_beta               0.00           0.00           0.00    0.0000   0.5639

Starting values for error model parameters:
a.1 b.1
  1   1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2249 2241  -1104

Optimised parameters:
                      est.      lower     upper
cyan_0            101.55265  9.920e+01  103.9059
log_k_JCZ38        -2.32302 -2.832e+00   -1.8142
log_k_J9Z38        -5.13082 -5.942e+00   -4.3199
log_k_JSE76        -3.01756 -4.262e+00   -1.7736
f_cyan_ilr_1        0.70850  3.657e-01    1.0513
f_cyan_ilr_2        0.95775  2.612e-01    1.6543
f_JCZ38_qlogis      3.86105  9.248e-01    6.7973
f_JSE76_qlogis      7.51583 -1.120e+02  127.0392
log_alpha          -0.15308 -4.508e-01    0.1446
log_beta            2.99165  2.711e+00    3.2720
a.1                 2.04034  1.843e+00    2.2382
```

```
b.1                0.06924  5.749e-02    0.0810
SD.log_k_JCZ38     0.50818  1.390e-01    0.8774
SD.log_k_J9Z38     0.86597  2.652e-01    1.4667
SD.log_k_JSE76     1.38092  4.864e-01    2.2754
SD.f_cyan_ilr_1    0.38204  1.354e-01    0.6286
SD.f_cyan_ilr_2    0.55129  7.198e-02    1.0306
SD.f_JCZ38_qlogis  1.88457  1.711e-02    3.7520
SD.f_JSE76_qlogis  2.64018 -2.450e+03 2454.9447
SD.log_alpha       0.31860  1.047e-01    0.5325
SD.log_beta        0.24195  1.273e-02    0.4712

Correlation:
               cyan_0  l__JCZ3 l__J9Z3 l__JSE7 f_cy__1 f_cy__2 f_JCZ38 f_JSE76
log_k_JCZ38    -0.0235
log_k_J9Z38    -0.0442  0.0047
log_k_JSE76    -0.0023  0.0966  0.0006
f_cyan_ilr_1   -0.0032  0.0070 -0.0536 -0.0001
f_cyan_ilr_2   -0.5189  0.0452  0.1152  0.0013 -0.0304
f_JCZ38_qlogis  0.1088 -0.0848 -0.0240  0.0040 -0.0384 -0.2303
f_JSE76_qlogis -0.0545  0.1315  0.0195  0.0020  0.0252  0.1737 -0.5939
log_alpha      -0.0445  0.0056  0.0261  0.0019 -0.0055  0.0586 -0.0239 -0.0284
log_beta       -0.2388  0.0163  0.0566  0.0040 -0.0078  0.2183 -0.0714 -0.0332
               log_lph
log_k_JCZ38
log_k_J9Z38
log_k_JSE76
f_cyan_ilr_1
f_cyan_ilr_2
f_JCZ38_qlogis
f_JSE76_qlogis
log_alpha
log_beta        0.2135

Random effects:
                    est.      lower     upper
SD.log_k_JCZ38    0.5082  1.390e-01    0.8774
SD.log_k_J9Z38    0.8660  2.652e-01    1.4667
SD.log_k_JSE76    1.3809  4.864e-01    2.2754
SD.f_cyan_ilr_1   0.3820  1.354e-01    0.6286
SD.f_cyan_ilr_2   0.5513  7.198e-02    1.0306
SD.f_JCZ38_qlogis 1.8846  1.711e-02    3.7520
SD.f_JSE76_qlogis 2.6402 -2.450e+03 2454.9447
SD.log_alpha      0.3186  1.047e-01    0.5325
SD.log_beta       0.2420  1.273e-02    0.4712

Variance model:
       est.   lower upper
a.1 2.04034 1.84252 2.238
b.1 0.06924 0.05749 0.081

Backtransformed parameters:
                      est.     lower    upper
cyan_0           1.016e+02 9.920e+01 103.9059
k_JCZ38          9.798e-02 5.890e-02   0.1630
k_J9Z38          5.912e-03 2.627e-03   0.0133
k_JSE76          4.892e-02 1.410e-02   0.1697
f_cyan_to_JCZ38  6.432e-01        NA       NA
f_cyan_to_J9Z38  2.362e-01        NA       NA
f_JCZ38_to_JSE76 9.794e-01 7.160e-01   0.9989
f_JSE76_to_JCZ38 9.995e-01 2.268e-49   1.0000
alpha            8.581e-01 6.371e-01   1.1556
beta             1.992e+01 1.505e+01  26.3646

Resulting formation fractions:
                   ff
cyan_JCZ38  0.6432301
cyan_J9Z38  0.2361657
cyan_sink   0.1206042
JCZ38_JSE76 0.9793879
JCZ38_sink  0.0206121
JSE76_JCZ38 0.9994559
JSE76_sink  0.0005441

Estimated disappearance times:
         DT50   DT90 DT50back
cyan   24.759 271.61    81.76
JCZ38   7.075  23.50       NA
J9Z38 117.249 389.49       NA
JSE76  14.169  47.07       NA
```

Listing 11: Hierarchical DFOP path 2 fit with constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:47:03 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
           time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
           * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
           g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
           exp(-k2 * time))) * cyan - k_JCZ38 * JCZ38 +
           f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_to_J9Z38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
           g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
           exp(-k2 * time))) * cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 567.679 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
       cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
     102.4380        -2.3107        -5.3123        -3.7120         0.6757
  f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis         log_k1         log_k2
       1.1439        13.1194        12.3492        -1.9317        -4.4557
     g_qlogis
      -0.5644

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          4.591      0.0000       0.000         0.0       0.0000
log_k_JCZ38     0.000      0.7966       0.000         0.0       0.0000
log_k_J9Z38     0.000      0.0000       1.561         0.0       0.0000
log_k_JSE76     0.000      0.0000       0.000         0.8       0.0000
f_cyan_ilr_1    0.000      0.0000       0.000         0.0       0.6349
f_cyan_ilr_2    0.000      0.0000       0.000         0.0       0.0000
f_JCZ38_qlogis  0.000      0.0000       0.000         0.0       0.0000
f_JSE76_qlogis  0.000      0.0000       0.000         0.0       0.0000
log_k1          0.000      0.0000       0.000         0.0       0.0000
log_k2          0.000      0.0000       0.000         0.0       0.0000
g_qlogis        0.000      0.0000       0.000         0.0       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis log_k1 log_k2
cyan_0                0.000           0.00           0.00  0.000 0.0000
log_k_JCZ38           0.000           0.00           0.00  0.000 0.0000
log_k_J9Z38           0.000           0.00           0.00  0.000 0.0000
log_k_JSE76           0.000           0.00           0.00  0.000 0.0000
f_cyan_ilr_1          0.000           0.00           0.00  0.000 0.0000
f_cyan_ilr_2          1.797           0.00           0.00  0.000 0.0000
f_JCZ38_qlogis        0.000          13.86           0.00  0.000 0.0000
f_JSE76_qlogis        0.000           0.00          13.91  0.000 0.0000
log_k1                0.000           0.00           0.00  1.106 0.0000
log_k2                0.000           0.00           0.00  0.000 0.6141
g_qlogis              0.000           0.00           0.00  0.000 0.0000
               g_qlogis
cyan_0            0.000
log_k_JCZ38       0.000
log_k_J9Z38       0.000
log_k_JSE76       0.000
f_cyan_ilr_1      0.000
f_cyan_ilr_2      0.000
f_JCZ38_qlogis    0.000
f_JSE76_qlogis    0.000
log_k1            0.000
log_k2            0.000
g_qlogis          1.595

Starting values for error model parameters:
a.1
  1
```

```
Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2288 2280  -1122

Optimised parameters:
                      est.      lower      upper
cyan_0            102.7204  1.014e+02  1.040e+02
log_k_JCZ38        -2.8925 -4.044e+00 -1.741e+00
log_k_J9Z38        -5.1430 -5.828e+00 -4.457e+00
log_k_JSE76        -3.5577 -4.174e+00 -2.941e+00
f_cyan_ilr_1        0.6929  3.788e-01  1.007e+00
f_cyan_ilr_2        0.6066  5.342e-02  1.160e+00
f_JCZ38_qlogis      9.8071 -2.819e+03  2.838e+03
f_JSE76_qlogis      2.2229  5.684e-01  3.877e+00
log_k1             -1.9339 -2.609e+00 -1.258e+00
log_k2             -4.4709 -4.935e+00 -4.007e+00
g_qlogis           -0.4987 -1.373e+00  3.757e-01
a.1                 2.7368  2.545e+00  2.928e+00
SD.log_k_JCZ38      1.2747  4.577e-01  2.092e+00
SD.log_k_J9Z38      0.6758  1.418e-01  1.210e+00
SD.log_k_JSE76      0.5869  1.169e-01  1.057e+00
SD.f_cyan_ilr_1     0.3392  1.161e-01  5.622e-01
SD.f_cyan_ilr_2     0.4200  8.501e-02  7.550e-01
SD.f_JCZ38_qlogis   0.8511 -1.137e+06  1.137e+06
SD.f_JSE76_qlogis   0.3767 -5.238e-01  1.277e+00
SD.log_k1           0.7475  2.601e-01  1.235e+00
SD.log_k2           0.5179  1.837e-01  8.521e-01
SD.g_qlogis         0.9817  3.553e-01  1.608e+00

Correlation:
                cyan_0  l__JCZ3 l__J9Z3 l__JSE7 f_cy__1 f_cy__2 f_JCZ38 f_JSE76
log_k_JCZ38    -0.0351
log_k_J9Z38    -0.0541  0.0043
log_k_JSE76    -0.0078  0.0900 -0.0014
f_cyan_ilr_1   -0.0249  0.0268 -0.0962  0.0000
f_cyan_ilr_2   -0.3560  0.0848  0.1545 -0.0022  0.0463
f_JCZ38_qlogis  0.2005 -0.1226 -0.0347  0.0514 -0.1840 -0.5906
f_JSE76_qlogis -0.1638  0.1307  0.0266  0.0001  0.1645  0.5181 -0.9297
log_k1          0.0881 -0.0071  0.0005 -0.0070 -0.0064 -0.0346  0.0316 -0.0341
log_k2          0.0238 -0.0003  0.0082 -0.0022 -0.0017 -0.0017 -0.0002 -0.0076
g_qlogis        0.0198 -0.0002 -0.0109  0.0034  0.0017 -0.0176  0.0044  0.0051
                log_k1  log_k2
log_k_JCZ38
log_k_J9Z38
log_k_JSE76
f_cyan_ilr_1
f_cyan_ilr_2
f_JCZ38_qlogis
f_JSE76_qlogis
log_k1
log_k2          0.0276
g_qlogis       -0.0283 -0.0309

Random effects:
                     est.      lower     upper
SD.log_k_JCZ38    1.2747  4.577e-01 2.092e+00
SD.log_k_J9Z38    0.6758  1.418e-01 1.210e+00
SD.log_k_JSE76    0.5869  1.169e-01 1.057e+00
SD.f_cyan_ilr_1   0.3392  1.161e-01 5.622e-01
SD.f_cyan_ilr_2   0.4200  8.501e-02 7.550e-01
SD.f_JCZ38_qlogis 0.8511 -1.137e+06 1.137e+06
SD.f_JSE76_qlogis 0.3767 -5.238e-01 1.277e+00
SD.log_k1         0.7475  2.601e-01 1.235e+00
SD.log_k2         0.5179  1.837e-01 8.521e-01
SD.g_qlogis       0.9817  3.553e-01 1.608e+00

Variance model:
     est. lower upper
a.1 2.737 2.545 2.928

Backtransformed parameters:
                       est.     lower     upper
cyan_0            102.72037 1.014e+02 104.00464
k_JCZ38             0.05544 1.752e-02   0.17539
k_J9Z38             0.00584 2.942e-03   0.01159
k_JSE76             0.02850 1.539e-02   0.05279
f_cyan_to_JCZ38     0.59995        NA        NA
f_cyan_to_J9Z38     0.22519        NA        NA
f_JCZ38_to_JSE76    0.99994 0.000e+00   1.00000
f_JSE76_to_JCZ38    0.90229 6.384e-01   0.97971
k1                  0.14459 7.357e-02   0.28414
k2                  0.01144 7.192e-03   0.01819
```

```
g                 0.37784 2.021e-01   0.59284

Resulting formation fractions:
                  ff
cyan_JCZ38  5.999e-01
cyan_J9Z38  2.252e-01
cyan_sink   1.749e-01
JCZ38_JSE76 9.999e-01
JCZ38_sink  5.506e-05
JSE76_JCZ38 9.023e-01
JSE76_sink  9.771e-02

Estimated disappearance times:
        DT50   DT90 DT50back DT50_k1 DT50_k2
cyan   21.93 159.83    48.11   4.794    60.6
JCZ38  12.50  41.53       NA      NA      NA
J9Z38 118.69 394.27       NA      NA      NA
JSE76  24.32  80.78       NA      NA      NA
```

Listing 12: Hierarchical DFOP path 2 fit with two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:49:50 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
           time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
           * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
           g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
           exp(-k2 * time))) * cyan - k_JCZ38 * JCZ38 +
           f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_to_J9Z38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
           g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
           exp(-k2 * time))) * cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 734.852 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
       cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
     101.7393        -1.4493        -5.0118        -2.1269         0.6720
  f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis         log_k1         log_k2
       7.3362        13.4423        13.2659        -2.0061        -4.5527
     g_qlogis
      -0.5806

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          5.604        0.00       0.000       0.000       0.0000
log_k_JCZ38     0.000        2.77       0.000       0.000       0.0000
log_k_J9Z38     0.000        0.00       1.662       0.000       0.0000
log_k_JSE76     0.000        0.00       0.000       5.021       0.0000
f_cyan_ilr_1    0.000        0.00       0.000       0.000       0.6519
f_cyan_ilr_2    0.000        0.00       0.000       0.000       0.0000
f_JCZ38_qlogis  0.000        0.00       0.000       0.000       0.0000
f_JSE76_qlogis  0.000        0.00       0.000       0.000       0.0000
log_k1          0.000        0.00       0.000       0.000       0.0000
log_k2          0.000        0.00       0.000       0.000       0.0000
g_qlogis        0.000        0.00       0.000       0.000       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis log_k1 log_k2
cyan_0                 0.00           0.00           0.00 0.0000 0.0000
log_k_JCZ38            0.00           0.00           0.00 0.0000 0.0000
log_k_J9Z38            0.00           0.00           0.00 0.0000 0.0000
log_k_JSE76            0.00           0.00           0.00 0.0000 0.0000
f_cyan_ilr_1           0.00           0.00           0.00 0.0000 0.0000
f_cyan_ilr_2          13.37           0.00           0.00 0.0000 0.0000
f_JCZ38_qlogis         0.00          14.21           0.00 0.0000 0.0000
f_JSE76_qlogis         0.00           0.00          14.58 0.0000 0.0000
log_k1                 0.00           0.00           0.00 0.8453 0.0000
log_k2                 0.00           0.00           0.00 0.0000 0.5969
g_qlogis               0.00           0.00           0.00 0.0000 0.0000
               g_qlogis
cyan_0             0.00
log_k_JCZ38        0.00
log_k_J9Z38        0.00
log_k_JSE76        0.00
f_cyan_ilr_1       0.00
f_cyan_ilr_2       0.00
f_JCZ38_qlogis     0.00
f_JSE76_qlogis     0.00
log_k1             0.00
log_k2             0.00
g_qlogis           1.69

Starting values for error model parameters:
a.1 b.1
  1   1
```

```
Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2234 2226  -1095

Optimised parameters:
                       est.     lower     upper
cyan_0            101.25496  99.14662 103.36331
log_k_JCZ38        -2.55593  -3.32972  -1.78215
log_k_J9Z38        -5.07103  -5.85423  -4.28783
log_k_JSE76        -3.25468  -4.17577  -2.33360
f_cyan_ilr_1        0.70139   0.35924   1.04355
f_cyan_ilr_2        1.07712   0.17789   1.97636
f_JCZ38_qlogis      3.57483   0.05990   7.08976
f_JSE76_qlogis      4.54884  -7.25628  16.35395
log_k1             -2.38201  -2.51639  -2.24763
log_k2             -4.66741  -4.91865  -4.41617
g_qlogis           -0.28446  -1.14192   0.57300
a.1                 2.05925   1.86481   2.25369
b.1                 0.06172   0.05062   0.07282
SD.log_k_JCZ38      0.81137   0.25296   1.36977
SD.log_k_J9Z38      0.83542   0.25395   1.41689
SD.log_k_JSE76      0.97903   0.30100   1.65707
SD.f_cyan_ilr_1     0.37878   0.13374   0.62382
SD.f_cyan_ilr_2     0.67274   0.10102   1.24446
SD.f_JCZ38_qlogis   1.35327  -0.42359   3.13012
SD.f_JSE76_qlogis   1.43956 -19.14972  22.02884
SD.log_k2           0.25329   0.07521   0.43138
SD.g_qlogis         0.95167   0.35149   1.55184

Correlation:
                cyan_0  l__JCZ3 l__J9Z3 l__JSE7 f_cy__1 f_cy__2 f_JCZ38 f_JSE76
log_k_JCZ38    -0.0265
log_k_J9Z38    -0.0392  0.0024
log_k_JSE76     0.0011  0.1220 -0.0016
f_cyan_ilr_1   -0.0161  0.0217 -0.0552  0.0034
f_cyan_ilr_2   -0.4718  0.0829  0.1102  0.0042  0.0095
f_JCZ38_qlogis  0.1609 -0.1318 -0.0277  0.0081 -0.1040 -0.4559
f_JSE76_qlogis -0.1289  0.1494  0.0219  0.0012  0.1004  0.4309 -0.8543
log_k1          0.2618 -0.0739 -0.0167 -0.0148 -0.0444 -0.2768  0.3518 -0.3818
log_k2          0.0603 -0.0217  0.0174 -0.0058 -0.0197 -0.0533  0.0923 -0.1281
g_qlogis        0.0362  0.0115 -0.0111  0.0040  0.0095 -0.0116 -0.0439  0.0651
                log_k1  log_k2
log_k_JCZ38
log_k_J9Z38
log_k_JSE76
f_cyan_ilr_1
f_cyan_ilr_2
f_JCZ38_qlogis
f_JSE76_qlogis
log_k1
log_k2          0.3269
g_qlogis       -0.1656 -0.0928

Random effects:
                     est.     lower   upper
SD.log_k_JCZ38     0.8114   0.25296  1.3698
SD.log_k_J9Z38     0.8354   0.25395  1.4169
SD.log_k_JSE76     0.9790   0.30100  1.6571
SD.f_cyan_ilr_1    0.3788   0.13374  0.6238
SD.f_cyan_ilr_2    0.6727   0.10102  1.2445
SD.f_JCZ38_qlogis 1.3533  -0.42359  3.1301
SD.f_JSE76_qlogis 1.4396 -19.14972 22.0288
SD.log_k2          0.2533   0.07521  0.4314
SD.g_qlogis        0.9517   0.35149  1.5518

Variance model:
       est.   lower   upper
a.1 2.05925 1.86481 2.25369
b.1 0.06172 0.05062 0.07282

Backtransformed parameters:
                        est.     lower     upper
cyan_0             1.013e+02 9.915e+01 103.36331
k_JCZ38            7.762e-02 3.580e-02   0.16828
k_J9Z38            6.276e-03 2.868e-03   0.01373
k_JSE76            3.859e-02 1.536e-02   0.09695
f_cyan_to_JCZ38    6.520e-01        NA        NA
f_cyan_to_J9Z38    2.418e-01        NA        NA
f_JCZ38_to_JSE76   9.727e-01 5.150e-01   0.99917
f_JSE76_to_JCZ38   9.895e-01 7.052e-04   1.00000
k1                 9.236e-02 8.075e-02   0.10565
k2                 9.397e-03 7.309e-03   0.01208
```

```
g               4.294e-01 2.420e-01   0.63945

Resulting formation fractions:
                ff
cyan_JCZ38  0.65203
cyan_J9Z38  0.24181
cyan_sink   0.10616
JCZ38_JSE76 0.97274
JCZ38_sink  0.02726
JSE76_JCZ38 0.98953
JSE76_sink  0.01047

Estimated disappearance times:
        DT50   DT90 DT50back DT50_k1 DT50_k2
cyan   24.26 185.34    55.79   7.504   73.77
JCZ38   8.93  29.66       NA      NA      NA
J9Z38 110.45 366.89       NA      NA      NA
JSE76  17.96  59.66       NA      NA      NA
```

Listing 13: Hierarchical SFORB path 2 fit with constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:47:00 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan_free/dt = - k_cyan_free * cyan_free - k_cyan_free_bound *
          cyan_free + k_cyan_bound_free * cyan_bound
d_cyan_bound/dt = + k_cyan_free_bound * cyan_free - k_cyan_bound_free *
          cyan_bound
d_JCZ38/dt = + f_cyan_free_to_JCZ38 * k_cyan_free * cyan_free - k_JCZ38
          * JCZ38 + f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_free_to_J9Z38 * k_cyan_free * cyan_free - k_J9Z38
          * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 564.736 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
          cyan_free_0       log_k_cyan_free log_k_cyan_free_bound
             102.4395               -2.7673               -2.8942
log_k_cyan_bound_free           log_k_JCZ38           log_k_J9Z38
              -3.6201               -2.3107               -5.3123
          log_k_JSE76          f_cyan_ilr_1          f_cyan_ilr_2
              -3.7120                0.6754                1.1448
       f_JCZ38_qlogis        f_JSE76_qlogis
             14.8408               15.4734

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                     cyan_free_0 log_k_cyan_free log_k_cyan_free_bound
cyan_free_0                4.589          0.0000                 0.00
log_k_cyan_free            0.000          0.4849                 0.00
log_k_cyan_free_bound      0.000          0.0000                 1.62
log_k_cyan_bound_free      0.000          0.0000                 0.00
log_k_JCZ38                0.000          0.0000                 0.00
log_k_J9Z38                0.000          0.0000                 0.00
log_k_JSE76                0.000          0.0000                 0.00
f_cyan_ilr_1               0.000          0.0000                 0.00
f_cyan_ilr_2               0.000          0.0000                 0.00
f_JCZ38_qlogis             0.000          0.0000                 0.00
f_JSE76_qlogis             0.000          0.0000                 0.00
                     log_k_cyan_bound_free log_k_JCZ38 log_k_J9Z38 log_k_JSE76
cyan_free_0                          0.000      0.0000       0.000         0.0
log_k_cyan_free                      0.000      0.0000       0.000         0.0
log_k_cyan_free_bound                0.000      0.0000       0.000         0.0
log_k_cyan_bound_free                1.197      0.0000       0.000         0.0
log_k_JCZ38                          0.000      0.7966       0.000         0.0
log_k_J9Z38                          0.000      0.0000       1.561         0.0
log_k_JSE76                          0.000      0.0000       0.000         0.8
f_cyan_ilr_1                         0.000      0.0000       0.000         0.0
f_cyan_ilr_2                         0.000      0.0000       0.000         0.0
f_JCZ38_qlogis                       0.000      0.0000       0.000         0.0
f_JSE76_qlogis                       0.000      0.0000       0.000         0.0
                     f_cyan_ilr_1 f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis
cyan_free_0                0.0000        0.000            0.0           0.00
log_k_cyan_free            0.0000        0.000            0.0           0.00
log_k_cyan_free_bound      0.0000        0.000            0.0           0.00
log_k_cyan_bound_free      0.0000        0.000            0.0           0.00
log_k_JCZ38                0.0000        0.000            0.0           0.00
log_k_J9Z38                0.0000        0.000            0.0           0.00
log_k_JSE76                0.0000        0.000            0.0           0.00
f_cyan_ilr_1               0.6349        0.000            0.0           0.00
f_cyan_ilr_2               0.0000        1.797            0.0           0.00
f_JCZ38_qlogis             0.0000        0.000           15.6           0.00
f_JSE76_qlogis             0.0000        0.000            0.0          17.52

Starting values for error model parameters:
a.1
  1
```

```
Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2283 2275  -1120

Optimised parameters:
                           est.     lower    upper
cyan_free_0              102.6517 101.40815 103.8952
log_k_cyan_free           -2.8729  -3.18649  -2.5593
log_k_cyan_free_bound     -2.7803  -3.60525  -1.9552
log_k_cyan_bound_free     -3.5845  -4.16644  -3.0026
log_k_JCZ38               -2.3411  -2.89698  -1.7852
log_k_J9Z38               -5.2487  -6.01271  -4.4847
log_k_JSE76               -3.0259  -4.28274  -1.7690
f_cyan_ilr_1               0.7289   0.38214   1.0756
f_cyan_ilr_2               0.6891   0.18277   1.1954
f_JCZ38_qlogis             4.2162   0.47015   7.9622
f_JSE76_qlogis             5.8911 -20.19088  31.9730
a.1                        2.7159   2.52587   2.9060
SD.log_k_cyan_free         0.3354   0.10979   0.5610
SD.log_k_cyan_free_bound   0.9061   0.30969   1.5025
SD.log_k_cyan_bound_free   0.6376   0.21229   1.0628
SD.log_k_JCZ38             0.5499   0.14533   0.9545
SD.log_k_J9Z38             0.7457   0.15106   1.3404
SD.log_k_JSE76             1.3822   0.47329   2.2912
SD.f_cyan_ilr_1            0.3820   0.13280   0.6313
SD.f_cyan_ilr_2            0.4317   0.06803   0.7953
SD.f_JCZ38_qlogis          1.8258  -0.25423   3.9059
SD.f_JSE76_qlogis          2.2348 -83.33679  87.8065

Correlation:
                        cyn_f_0 lg_k_c_ lg_k_cyn_f_ lg_k_cyn_b_ l__JCZ3 l__J9Z3
log_k_cyan_free          0.1944
log_k_cyan_free_bound    0.0815  0.0814
log_k_cyan_bound_free    0.0106  0.0426  0.0585
log_k_JCZ38             -0.0231 -0.0106 -0.0089     -0.0051
log_k_J9Z38             -0.0457 -0.0108  0.0019      0.0129      0.0032
log_k_JSE76             -0.0054 -0.0024 -0.0017     -0.0005      0.1108  0.0009
f_cyan_ilr_1             0.0051 -0.0005 -0.0035     -0.0056      0.0131 -0.0967
f_cyan_ilr_2            -0.3182 -0.0771 -0.0309     -0.0038      0.0680  0.1643
f_JCZ38_qlogis           0.0834  0.0369  0.0302      0.0172     -0.1145 -0.0204
f_JSE76_qlogis          -0.0553 -0.0365 -0.0441     -0.0414      0.1579  0.0175
                        l__JSE7 f_cy__1 f_cy__2 f_JCZ38
log_k_cyan_free
log_k_cyan_free_bound
log_k_cyan_bound_free
log_k_JCZ38
log_k_J9Z38
log_k_JSE76
f_cyan_ilr_1            -0.0002
f_cyan_ilr_2             0.0020 -0.0415
f_JCZ38_qlogis           0.0052 -0.0665 -0.3437
f_JSE76_qlogis           0.0066  0.0635  0.3491 -0.7487

Random effects:
                             est.     lower   upper
SD.log_k_cyan_free         0.3354   0.10979  0.5610
SD.log_k_cyan_free_bound   0.9061   0.30969  1.5025
SD.log_k_cyan_bound_free   0.6376   0.21229  1.0628
SD.log_k_JCZ38             0.5499   0.14533  0.9545
SD.log_k_J9Z38             0.7457   0.15106  1.3404
SD.log_k_JSE76             1.3822   0.47329  2.2912
SD.f_cyan_ilr_1            0.3820   0.13280  0.6313
SD.f_cyan_ilr_2            0.4317   0.06803  0.7953
SD.f_JCZ38_qlogis          1.8258  -0.25423  3.9059
SD.f_JSE76_qlogis          2.2348 -83.33679 87.8065

Variance model:
     est. lower upper
a.1 2.716 2.526 2.906

Backtransformed parameters:
                            est.     lower     upper
cyan_free_0           1.027e+02 1.014e+02 103.89517
k_cyan_free           5.654e-02 4.132e-02   0.07736
k_cyan_free_bound     6.202e-02 2.718e-02   0.14153
k_cyan_bound_free     2.775e-02 1.551e-02   0.04966
k_JCZ38               9.622e-02 5.519e-02   0.16777
k_J9Z38               5.254e-03 2.447e-03   0.01128
k_JSE76               4.852e-02 1.380e-02   0.17051
f_cyan_free_to_JCZ38  6.197e-01 5.643e-01   0.84429
f_cyan_free_to_J9Z38  2.211e-01 5.643e-01   0.84429
f_JCZ38_to_JSE76      9.855e-01 6.154e-01   0.99965
```

```
f_JSE76_to_JCZ38     9.972e-01 1.703e-09   1.00000

Estimated Eigenvalues of SFORB model(s):
cyan_b1 cyan_b2  cyan_g
0.13466 0.01165 0.36490

Resulting formation fractions:
                      ff
cyan_free_JCZ38 0.619745
cyan_free_J9Z38 0.221083
cyan_free_sink  0.159172
cyan_free       1.000000
JCZ38_JSE76     0.985460
JCZ38_sink      0.014540
JSE76_JCZ38     0.997244
JSE76_sink      0.002756

Estimated disappearance times:
         DT50   DT90 DT50back DT50_cyan_b1 DT50_cyan_b2
cyan   23.293 158.67    47.77        5.147         59.5
JCZ38   7.203  23.93       NA           NA           NA
J9Z38 131.918 438.22       NA           NA           NA
JSE76  14.287  47.46       NA           NA           NA
```

Listing 14: Hierarchical SFORB path 2 fit with two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 18:49:47 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan_free/dt = - k_cyan_free * cyan_free - k_cyan_free_bound *
          cyan_free + k_cyan_bound_free * cyan_bound
d_cyan_bound/dt = + k_cyan_free_bound * cyan_free - k_cyan_bound_free *
          cyan_bound
d_JCZ38/dt = + f_cyan_free_to_JCZ38 * k_cyan_free * cyan_free - k_JCZ38
          * JCZ38 + f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_free_to_J9Z38 * k_cyan_free * cyan_free - k_J9Z38
          * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 731.571 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
          cyan_free_0       log_k_cyan_free log_k_cyan_free_bound
            101.7511               -2.8370               -3.0162
log_k_cyan_bound_free           log_k_JCZ38           log_k_J9Z38
             -3.6600               -2.2988               -5.3129
          log_k_JSE76          f_cyan_ilr_1          f_cyan_ilr_2
             -3.6991                0.6722                4.8596
       f_JCZ38_qlogis        f_JSE76_qlogis
              13.4678               14.2149

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                     cyan_free_0 log_k_cyan_free log_k_cyan_free_bound
cyan_free_0                5.629           0.000                 0.000
log_k_cyan_free            0.000           0.446                 0.000
log_k_cyan_free_bound      0.000           0.000                 1.449
log_k_cyan_bound_free      0.000           0.000                 0.000
log_k_JCZ38                0.000           0.000                 0.000
log_k_J9Z38                0.000           0.000                 0.000
log_k_JSE76                0.000           0.000                 0.000
f_cyan_ilr_1               0.000           0.000                 0.000
f_cyan_ilr_2               0.000           0.000                 0.000
f_JCZ38_qlogis             0.000           0.000                 0.000
f_JSE76_qlogis             0.000           0.000                 0.000
                     log_k_cyan_bound_free log_k_JCZ38 log_k_J9Z38 log_k_JSE76
cyan_free_0                          0.000      0.0000       0.000      0.0000
log_k_cyan_free                      0.000      0.0000       0.000      0.0000
log_k_cyan_free_bound                0.000      0.0000       0.000      0.0000
log_k_cyan_bound_free                1.213      0.0000       0.000      0.0000
log_k_JCZ38                          0.000      0.7801       0.000      0.0000
log_k_J9Z38                          0.000      0.0000       1.575      0.0000
log_k_JSE76                          0.000      0.0000       0.000      0.8078
f_cyan_ilr_1                         0.000      0.0000       0.000      0.0000
f_cyan_ilr_2                         0.000      0.0000       0.000      0.0000
f_JCZ38_qlogis                       0.000      0.0000       0.000      0.0000
f_JSE76_qlogis                       0.000      0.0000       0.000      0.0000
                     f_cyan_ilr_1 f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis
cyan_free_0                0.0000        0.000           0.00           0.00
log_k_cyan_free            0.0000        0.000           0.00           0.00
log_k_cyan_free_bound      0.0000        0.000           0.00           0.00
log_k_cyan_bound_free      0.0000        0.000           0.00           0.00
log_k_JCZ38                0.0000        0.000           0.00           0.00
log_k_J9Z38                0.0000        0.000           0.00           0.00
log_k_JSE76                0.0000        0.000           0.00           0.00
f_cyan_ilr_1               0.6518        0.000           0.00           0.00
f_cyan_ilr_2               0.0000        9.981           0.00           0.00
f_JCZ38_qlogis             0.0000        0.000          14.26           0.00
f_JSE76_qlogis             0.0000        0.000           0.00          16.17

Starting values for error model parameters:
a.1 b.1
  1   1
```

```
Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2240 2231  -1098

Optimised parameters:
                           est.      lower      upper
cyan_free_0              100.73014  9.873e+01  1.027e+02
log_k_cyan_free           -3.19634 -3.641e+00 -2.752e+00
log_k_cyan_free_bound     -3.43533 -3.674e+00 -3.197e+00
log_k_cyan_bound_free     -3.83282 -4.163e+00 -3.503e+00
log_k_JCZ38               -2.51065 -3.225e+00 -1.796e+00
log_k_J9Z38               -5.02539 -5.825e+00 -4.226e+00
log_k_JSE76               -3.24777 -4.163e+00 -2.333e+00
f_cyan_ilr_1               0.70640  3.562e-01  1.057e+00
f_cyan_ilr_2               1.42704  3.170e-01  2.537e+00
f_JCZ38_qlogis             2.84779  1.042e+00  4.654e+00
f_JSE76_qlogis             8.63674 -6.407e+02  6.580e+02
a.1                        2.07082  1.877e+00  2.265e+00
b.1                        0.06227  5.098e-02  7.355e-02
SD.log_k_cyan_free         0.49674  1.865e-01  8.069e-01
SD.log_k_cyan_bound_free   0.28537  6.809e-02  5.027e-01
SD.log_k_JCZ38             0.74846  2.305e-01  1.266e+00
SD.log_k_J9Z38             0.86077  2.713e-01  1.450e+00
SD.log_k_JSE76             0.97613  3.030e-01  1.649e+00
SD.f_cyan_ilr_1            0.38994  1.382e-01  6.417e-01
SD.f_cyan_ilr_2            0.82869  3.917e-02  1.618e+00
SD.f_JCZ38_qlogis          1.05000 -2.808e-02  2.128e+00
SD.f_JSE76_qlogis          0.44681 -3.985e+05  3.985e+05

Correlation:
                        cyn_f_0 lg_k_c_ lg_k_cyn_f_ lg_k_cyn_b_ l__JCZ3 l__J9Z3
log_k_cyan_free          0.0936
log_k_cyan_free_bound    0.1302  0.1627
log_k_cyan_bound_free    0.0029  0.0525  0.5181
log_k_JCZ38             -0.0116 -0.0077 -0.0430     -0.0236
log_k_J9Z38             -0.0192 -0.0077 -0.0048      0.0229     -0.0005
log_k_JSE76              0.0007 -0.0020 -0.0134     -0.0072      0.1225 -0.0016
f_cyan_ilr_1            -0.0118 -0.0027 -0.0132     -0.0118      0.0127 -0.0505
f_cyan_ilr_2            -0.4643 -0.0762 -0.1245      0.0137      0.0497  0.1003
f_JCZ38_qlogis           0.0710  0.0371  0.1826      0.0925     -0.0869 -0.0130
f_JSE76_qlogis          -0.0367 -0.0270 -0.2274     -0.1865      0.1244  0.0098
                        l__JSE7 f_cy__1 f_cy__2 f_JCZ38
log_k_cyan_free
log_k_cyan_free_bound
log_k_cyan_bound_free
log_k_JCZ38
log_k_J9Z38
log_k_JSE76
f_cyan_ilr_1             0.0036
f_cyan_ilr_2             0.0050 -0.0201
f_JCZ38_qlogis           0.0142 -0.0529 -0.2698
f_JSE76_qlogis           0.0064  0.0345  0.2015 -0.7058

Random effects:
                             est.      lower     upper
SD.log_k_cyan_free       0.4967  1.865e-01 8.069e-01
SD.log_k_cyan_bound_free 0.2854  6.809e-02 5.027e-01
SD.log_k_JCZ38           0.7485  2.305e-01 1.266e+00
SD.log_k_J9Z38           0.8608  2.713e-01 1.450e+00
SD.log_k_JSE76           0.9761  3.030e-01 1.649e+00
SD.f_cyan_ilr_1          0.3899  1.382e-01 6.417e-01
SD.f_cyan_ilr_2          0.8287  3.917e-02 1.618e+00
SD.f_JCZ38_qlogis        1.0500 -2.808e-02 2.128e+00
SD.f_JSE76_qlogis        0.4468 -3.985e+05 3.985e+05

Variance model:
       est.   lower   upper
a.1 2.07082 1.87680 2.26483
b.1 0.06227 0.05098 0.07355

Backtransformed parameters:
                          est.      lower     upper
cyan_free_0          1.007e+02  9.873e+01 102.72898
k_cyan_free          4.091e-02  2.623e-02   0.06382
k_cyan_free_bound    3.221e-02  2.537e-02   0.04090
k_cyan_bound_free    2.165e-02  1.557e-02   0.03011
k_JCZ38              8.122e-02  3.975e-02   0.16594
k_J9Z38              6.569e-03  2.954e-03   0.01461
k_JSE76              3.886e-02  1.556e-02   0.09703
f_cyan_free_to_JCZ38 6.785e-01  6.102e-01   0.97309
f_cyan_free_to_J9Z38 2.498e-01  6.102e-01   0.97309
f_JCZ38_to_JSE76     9.452e-01  7.392e-01   0.99056
```

```
f_JSE76_to_JCZ38     9.998e-01 5.580e-279   1.00000

Estimated Eigenvalues of SFORB model(s):
cyan_b1 cyan_b2  cyan_g
0.08426 0.01051 0.41220

Resulting formation fractions:
                      ff
cyan_free_JCZ38 0.6784541
cyan_free_J9Z38 0.2498405
cyan_free_sink  0.0717054
cyan_free       1.0000000
JCZ38_JSE76     0.9452043
JCZ38_sink      0.0547957
JSE76_JCZ38     0.9998226
JSE76_sink      0.0001774

Estimated disappearance times:
         DT50   DT90 DT50back DT50_cyan_b1 DT50_cyan_b2
cyan   25.237 168.51    50.73        8.226        65.95
JCZ38   8.535  28.35       NA           NA           NA
J9Z38 105.517 350.52       NA           NA           NA
JSE76  17.837  59.25       NA           NA           NA
```

Pathway 2, refined fits

Listing 15: Hierarchical FOMC path 2 fit with reduced random effects, two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 19:03:34 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - (alpha/beta) * 1/((time/beta) + 1) * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * (alpha/beta) * 1/((time/beta) + 1) *
           cyan - k_JCZ38 * JCZ38 + f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_to_J9Z38 * (alpha/beta) * 1/((time/beta) + 1) *
           cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 821.812 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
        cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
      102.4477        -1.8631        -5.1087        -2.5114         0.6826
  f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis      log_alpha       log_beta
        4.7944        15.9616        13.1566        -0.1564         2.9781

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          7.701       0.000       0.000       0.000       0.0000
log_k_JCZ38     0.000       1.448       0.000       0.000       0.0000
log_k_J9Z38     0.000       0.000       1.724       0.000       0.0000
log_k_JSE76     0.000       0.000       0.000       3.659       0.0000
f_cyan_ilr_1    0.000       0.000       0.000       0.000       0.6356
f_cyan_ilr_2    0.000       0.000       0.000       0.000       0.0000
f_JCZ38_qlogis  0.000       0.000       0.000       0.000       0.0000
f_JSE76_qlogis  0.000       0.000       0.000       0.000       0.0000
log_alpha       0.000       0.000       0.000       0.000       0.0000
log_beta        0.000       0.000       0.000       0.000       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis log_alpha log_beta
cyan_0                 0.00           0.00           0.00    0.0000   0.0000
log_k_JCZ38            0.00           0.00           0.00    0.0000   0.0000
log_k_J9Z38            0.00           0.00           0.00    0.0000   0.0000
log_k_JSE76            0.00           0.00           0.00    0.0000   0.0000
f_cyan_ilr_1           0.00           0.00           0.00    0.0000   0.0000
f_cyan_ilr_2          10.32           0.00           0.00    0.0000   0.0000
f_JCZ38_qlogis         0.00          12.23           0.00    0.0000   0.0000
f_JSE76_qlogis         0.00           0.00          14.99    0.0000   0.0000
log_alpha              0.00           0.00           0.00    0.3924   0.0000
log_beta               0.00           0.00           0.00    0.0000   0.5639

Starting values for error model parameters:
a.1 b.1
  1   1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2249 2242  -1106

Optimised parameters:
                    est.   lower  upper
cyan_0          101.24524      NA     NA
log_k_JCZ38      -2.85375      NA     NA
log_k_J9Z38      -5.07729      NA     NA
log_k_JSE76      -3.53511      NA     NA
f_cyan_ilr_1      0.67478      NA     NA
f_cyan_ilr_2      0.97152      NA     NA
f_JCZ38_qlogis  213.48001      NA     NA
f_JSE76_qlogis    2.02040      NA     NA
log_alpha        -0.11041      NA     NA
log_beta          3.06575      NA     NA
a.1               2.05279 1.85495 2.2506
```

```
b.1               0.07116 0.05912 0.0832
SD.log_k_JCZ38    1.21713 0.44160 1.9927
SD.log_k_J9Z38    0.88268 0.27541 1.4900
SD.log_k_JSE76    0.59452 0.15005 1.0390
SD.f_cyan_ilr_1   0.35370 0.12409 0.5833
SD.f_cyan_ilr_2   0.78186 0.18547 1.3782
SD.log_alpha      0.27781 0.08168 0.4739
SD.log_beta       0.32608 0.06490 0.5873

Correlation is not available

Random effects:
                  est.   lower  upper
SD.log_k_JCZ38  1.2171 0.44160 1.9927
SD.log_k_J9Z38  0.8827 0.27541 1.4900
SD.log_k_JSE76  0.5945 0.15005 1.0390
SD.f_cyan_ilr_1 0.3537 0.12409 0.5833
SD.f_cyan_ilr_2 0.7819 0.18547 1.3782
SD.log_alpha    0.2778 0.08168 0.4739
SD.log_beta     0.3261 0.06490 0.5873

Variance model:
       est.   lower  upper
a.1 2.05279 1.85495 2.2506
b.1 0.07116 0.05912 0.0832

Backtransformed parameters:
                      est. lower upper
cyan_0           1.012e+02    NA    NA
k_JCZ38          5.763e-02    NA    NA
k_J9Z38          6.237e-03    NA    NA
k_JSE76          2.916e-02    NA    NA
f_cyan_to_JCZ38  6.354e-01    NA    NA
f_cyan_to_J9Z38  2.447e-01    NA    NA
f_JCZ38_to_JSE76 1.000e+00    NA    NA
f_JSE76_to_JCZ38 8.829e-01    NA    NA
alpha            8.955e-01    NA    NA
beta             2.145e+01    NA    NA

Resulting formation fractions:
                ff
cyan_JCZ38  0.6354
cyan_J9Z38  0.2447
cyan_sink   0.1200
JCZ38_JSE76 1.0000
JCZ38_sink  0.0000
JSE76_JCZ38 0.8829
JSE76_sink  0.1171

Estimated disappearance times:
        DT50   DT90 DT50back
cyan   25.07 259.21    78.03
JCZ38  12.03  39.96       NA
J9Z38 111.14 369.19       NA
JSE76  23.77  78.98       NA
```

Listing 16: Hierarchical DFOP path 2 fit with reduced random effects, constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 19:05:19 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
            time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
            * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
            g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
            exp(-k2 * time))) * cyan - k_JCZ38 * JCZ38 +
            f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_to_J9Z38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
            g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
            exp(-k2 * time))) * cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 926.471 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
       cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
     102.4380        -2.3107        -5.3123        -3.7120         0.6757
  f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis         log_k1         log_k2
       1.1439        13.1194        12.3492        -1.9317        -4.4557
     g_qlogis
      -0.5644

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          4.591      0.0000       0.000         0.0       0.0000
log_k_JCZ38     0.000      0.7966       0.000         0.0       0.0000
log_k_J9Z38     0.000      0.0000       1.561         0.0       0.0000
log_k_JSE76     0.000      0.0000       0.000         0.8       0.0000
f_cyan_ilr_1    0.000      0.0000       0.000         0.0       0.6349
f_cyan_ilr_2    0.000      0.0000       0.000         0.0       0.0000
f_JCZ38_qlogis  0.000      0.0000       0.000         0.0       0.0000
f_JSE76_qlogis  0.000      0.0000       0.000         0.0       0.0000
log_k1          0.000      0.0000       0.000         0.0       0.0000
log_k2          0.000      0.0000       0.000         0.0       0.0000
g_qlogis        0.000      0.0000       0.000         0.0       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis log_k1 log_k2
cyan_0                0.000           0.00           0.00  0.000 0.0000
log_k_JCZ38           0.000           0.00           0.00  0.000 0.0000
log_k_J9Z38           0.000           0.00           0.00  0.000 0.0000
log_k_JSE76           0.000           0.00           0.00  0.000 0.0000
f_cyan_ilr_1          0.000           0.00           0.00  0.000 0.0000
f_cyan_ilr_2          1.797           0.00           0.00  0.000 0.0000
f_JCZ38_qlogis        0.000          13.86           0.00  0.000 0.0000
f_JSE76_qlogis        0.000           0.00          13.91  0.000 0.0000
log_k1                0.000           0.00           0.00  1.106 0.0000
log_k2                0.000           0.00           0.00  0.000 0.6141
g_qlogis              0.000           0.00           0.00  0.000 0.0000
               g_qlogis
cyan_0            0.000
log_k_JCZ38       0.000
log_k_J9Z38       0.000
log_k_JSE76       0.000
f_cyan_ilr_1      0.000
f_cyan_ilr_2      0.000
f_JCZ38_qlogis    0.000
f_JSE76_qlogis    0.000
log_k1            0.000
log_k2            0.000
g_qlogis          1.595

Starting values for error model parameters:
a.1
  1
```

```
Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2282 2274  -1121

Optimised parameters:
                    est.   lower  upper
cyan_0           102.6036      NA     NA
log_k_JCZ38       -2.9348      NA     NA
log_k_J9Z38       -5.1617      NA     NA
log_k_JSE76       -3.6396      NA     NA
f_cyan_ilr_1       0.6991      NA     NA
f_cyan_ilr_2       0.6341      NA     NA
f_JCZ38_qlogis  4232.3011      NA     NA
f_JSE76_qlogis     1.9658      NA     NA
log_k1            -1.9503      NA     NA
log_k2            -4.4745      NA     NA
g_qlogis          -0.4967      NA     NA
a.1                2.7461 2.59274 2.8994
SD.log_k_JCZ38     1.3178 0.47602 2.1596
SD.log_k_J9Z38     0.7022 0.15061 1.2538
SD.log_k_JSE76     0.6566 0.15613 1.1570
SD.f_cyan_ilr_1    0.3409 0.11666 0.5652
SD.f_cyan_ilr_2    0.4385 0.09482 0.7821
SD.log_k1          0.7381 0.25599 1.2202
SD.log_k2          0.5133 0.18152 0.8450
SD.g_qlogis        0.9866 0.35681 1.6164

Correlation is not available

Random effects:
                   est.   lower  upper
SD.log_k_JCZ38  1.3178 0.47602 2.1596
SD.log_k_J9Z38  0.7022 0.15061 1.2538
SD.log_k_JSE76  0.6566 0.15613 1.1570
SD.f_cyan_ilr_1 0.3409 0.11666 0.5652
SD.f_cyan_ilr_2 0.4385 0.09482 0.7821
SD.log_k1       0.7381 0.25599 1.2202
SD.log_k2       0.5133 0.18152 0.8450
SD.g_qlogis     0.9866 0.35681 1.6164

Variance model:
     est. lower upper
a.1 2.746 2.593 2.899

Backtransformed parameters:
                       est. lower upper
cyan_0            1.026e+02    NA    NA
k_JCZ38           5.314e-02    NA    NA
k_J9Z38           5.732e-03    NA    NA
k_JSE76           2.626e-02    NA    NA
f_cyan_to_JCZ38   6.051e-01    NA    NA
f_cyan_to_J9Z38   2.251e-01    NA    NA
f_JCZ38_to_JSE76  1.000e+00    NA    NA
f_JSE76_to_JCZ38  8.772e-01    NA    NA
k1                1.422e-01    NA    NA
k2                1.140e-02    NA    NA
g                 3.783e-01    NA    NA

Resulting formation fractions:
                  ff
cyan_JCZ38   0.6051
cyan_J9Z38   0.2251
cyan_sink    0.1698
JCZ38_JSE76  1.0000
JCZ38_sink   0.0000
JSE76_JCZ38  0.8772
JSE76_sink   0.1228

Estimated disappearance times:
        DT50   DT90 DT50back DT50_k1 DT50_k2
cyan   22.05 160.35    48.27   4.873   60.83
JCZ38  13.04  43.33       NA      NA      NA
J9Z38 120.93 401.73       NA      NA      NA
JSE76  26.39  87.68       NA      NA      NA
```

Listing 17: Hierarchical DFOP path 2 fit with reduced random effects, two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 19:05:53 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
            time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
            * cyan
d_JCZ38/dt = + f_cyan_to_JCZ38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
            g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
            exp(-k2 * time))) * cyan - k_JCZ38 * JCZ38 +
            f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_to_J9Z38 * ((k1 * g * exp(-k1 * time) + k2 * (1 -
            g) * exp(-k2 * time)) / (g * exp(-k1 * time) + (1 - g) *
            exp(-k2 * time))) * cyan - k_J9Z38 * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 961.025 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
       cyan_0    log_k_JCZ38    log_k_J9Z38    log_k_JSE76   f_cyan_ilr_1
     101.7393        -1.4493        -5.0118        -2.1269         0.6720
  f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis         log_k1         log_k2
       7.3362        13.4423        13.2659        -2.0061        -4.5527
     g_qlogis
      -0.5806

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
               cyan_0 log_k_JCZ38 log_k_J9Z38 log_k_JSE76 f_cyan_ilr_1
cyan_0          5.604        0.00       0.000       0.000       0.0000
log_k_JCZ38     0.000        2.77       0.000       0.000       0.0000
log_k_J9Z38     0.000        0.00       1.662       0.000       0.0000
log_k_JSE76     0.000        0.00       0.000       5.021       0.0000
f_cyan_ilr_1    0.000        0.00       0.000       0.000       0.6519
f_cyan_ilr_2    0.000        0.00       0.000       0.000       0.0000
f_JCZ38_qlogis  0.000        0.00       0.000       0.000       0.0000
f_JSE76_qlogis  0.000        0.00       0.000       0.000       0.0000
log_k1          0.000        0.00       0.000       0.000       0.0000
log_k2          0.000        0.00       0.000       0.000       0.0000
g_qlogis        0.000        0.00       0.000       0.000       0.0000
               f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis log_k1 log_k2
cyan_0                 0.00           0.00           0.00 0.0000 0.0000
log_k_JCZ38            0.00           0.00           0.00 0.0000 0.0000
log_k_J9Z38            0.00           0.00           0.00 0.0000 0.0000
log_k_JSE76            0.00           0.00           0.00 0.0000 0.0000
f_cyan_ilr_1           0.00           0.00           0.00 0.0000 0.0000
f_cyan_ilr_2          13.37           0.00           0.00 0.0000 0.0000
f_JCZ38_qlogis         0.00          14.21           0.00 0.0000 0.0000
f_JSE76_qlogis         0.00           0.00          14.58 0.0000 0.0000
log_k1                 0.00           0.00           0.00 0.8453 0.0000
log_k2                 0.00           0.00           0.00 0.0000 0.5969
g_qlogis               0.00           0.00           0.00 0.0000 0.0000
               g_qlogis
cyan_0             0.00
log_k_JCZ38        0.00
log_k_J9Z38        0.00
log_k_JSE76        0.00
f_cyan_ilr_1       0.00
f_cyan_ilr_2       0.00
f_JCZ38_qlogis     0.00
f_JSE76_qlogis     0.00
log_k1             0.00
log_k2             0.00
g_qlogis           1.69

Starting values for error model parameters:
a.1 b.1
  1   1
```

```
Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2237 2229  -1099

Optimised parameters:
                    est.   lower   upper
cyan_0          101.00243      NA      NA
log_k_JCZ38      -2.80828      NA      NA
log_k_J9Z38      -5.04449      NA      NA
log_k_JSE76      -3.66981      NA      NA
f_cyan_ilr_1      0.72564      NA      NA
f_cyan_ilr_2      1.37978      NA      NA
f_JCZ38_qlogis    1.98726      NA      NA
f_JSE76_qlogis  414.80884      NA      NA
log_k1           -2.38601      NA      NA
log_k2           -4.63632      NA      NA
g_qlogis         -0.33920      NA      NA
a.1               2.10837 1.91261 2.30413
b.1               0.06223 0.05085 0.07361
SD.log_k_JCZ38    1.30902 0.48128 2.13675
SD.log_k_J9Z38    0.83882 0.25790 1.41974
SD.log_k_JSE76    0.58104 0.14201 1.02008
SD.f_cyan_ilr_1   0.35421 0.12398 0.58443
SD.f_cyan_ilr_2   0.79373 0.12007 1.46739
SD.log_k2         0.27476 0.08557 0.46394
SD.g_qlogis       0.96170 0.35463 1.56878

Correlation is not available

Random effects:
                  est.   lower  upper
SD.log_k_JCZ38  1.3090 0.48128 2.1367
SD.log_k_J9Z38  0.8388 0.25790 1.4197
SD.log_k_JSE76  0.5810 0.14201 1.0201
SD.f_cyan_ilr_1 0.3542 0.12398 0.5844
SD.f_cyan_ilr_2 0.7937 0.12007 1.4674
SD.log_k2       0.2748 0.08557 0.4639
SD.g_qlogis     0.9617 0.35463 1.5688

Variance model:
       est.   lower   upper
a.1 2.10837 1.91261 2.30413
b.1 0.06223 0.05085 0.07361

Backtransformed parameters:
                      est. lower upper
cyan_0           1.010e+02    NA    NA
k_JCZ38          6.031e-02    NA    NA
k_J9Z38          6.445e-03    NA    NA
k_JSE76          2.548e-02    NA    NA
f_cyan_to_JCZ38  6.808e-01    NA    NA
f_cyan_to_J9Z38  2.440e-01    NA    NA
f_JCZ38_to_JSE76 8.795e-01    NA    NA
f_JSE76_to_JCZ38 1.000e+00    NA    NA
k1               9.200e-02    NA    NA
k2               9.693e-03    NA    NA
g                4.160e-01    NA    NA

Resulting formation fractions:
                  ff
cyan_JCZ38  0.68081
cyan_J9Z38  0.24398
cyan_sink   0.07521
JCZ38_JSE76 0.87945
JCZ38_sink  0.12055
JSE76_JCZ38 1.00000
JSE76_sink  0.00000

Estimated disappearance times:
        DT50   DT90 DT50back DT50_k1 DT50_k2
cyan   25.00 182.05     54.8   7.535   71.51
JCZ38  11.49  38.18       NA      NA      NA
J9Z38 107.55 357.28       NA      NA      NA
JSE76  27.20  90.36       NA      NA      NA
```

Listing 18: Hierarchical SFORB path 2 fit with reduced random effects, constant variance

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 19:05:30 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan_free/dt = - k_cyan_free * cyan_free - k_cyan_free_bound *
          cyan_free + k_cyan_bound_free * cyan_bound
d_cyan_bound/dt = + k_cyan_free_bound * cyan_free - k_cyan_bound_free *
          cyan_bound
d_JCZ38/dt = + f_cyan_free_to_JCZ38 * k_cyan_free * cyan_free - k_JCZ38
          * JCZ38 + f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_free_to_J9Z38 * k_cyan_free * cyan_free - k_J9Z38
          * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 937.91 s
Using 300, 100 iterations and 10 chains

Variance model: Constant variance

Starting values for degradation parameters:
          cyan_free_0       log_k_cyan_free log_k_cyan_free_bound
             102.4395               -2.7673               -2.8942
log_k_cyan_bound_free           log_k_JCZ38           log_k_J9Z38
              -3.6201               -2.3107               -5.3123
          log_k_JSE76          f_cyan_ilr_1          f_cyan_ilr_2
              -3.7120                0.6754                1.1448
       f_JCZ38_qlogis        f_JSE76_qlogis
             14.8408               15.4734

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                     cyan_free_0 log_k_cyan_free log_k_cyan_free_bound
cyan_free_0                4.589          0.0000                 0.00
log_k_cyan_free            0.000          0.4849                 0.00
log_k_cyan_free_bound      0.000          0.0000                 1.62
log_k_cyan_bound_free      0.000          0.0000                 0.00
log_k_JCZ38                0.000          0.0000                 0.00
log_k_J9Z38                0.000          0.0000                 0.00
log_k_JSE76                0.000          0.0000                 0.00
f_cyan_ilr_1               0.000          0.0000                 0.00
f_cyan_ilr_2               0.000          0.0000                 0.00
f_JCZ38_qlogis             0.000          0.0000                 0.00
f_JSE76_qlogis             0.000          0.0000                 0.00
                     log_k_cyan_bound_free log_k_JCZ38 log_k_J9Z38 log_k_JSE76
cyan_free_0                          0.000      0.0000       0.000         0.0
log_k_cyan_free                      0.000      0.0000       0.000         0.0
log_k_cyan_free_bound                0.000      0.0000       0.000         0.0
log_k_cyan_bound_free                1.197      0.0000       0.000         0.0
log_k_JCZ38                          0.000      0.7966       0.000         0.0
log_k_J9Z38                          0.000      0.0000       1.561         0.0
log_k_JSE76                          0.000      0.0000       0.000         0.8
f_cyan_ilr_1                         0.000      0.0000       0.000         0.0
f_cyan_ilr_2                         0.000      0.0000       0.000         0.0
f_JCZ38_qlogis                       0.000      0.0000       0.000         0.0
f_JSE76_qlogis                       0.000      0.0000       0.000         0.0
                     f_cyan_ilr_1 f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis
cyan_free_0                0.0000        0.000            0.0           0.00
log_k_cyan_free            0.0000        0.000            0.0           0.00
log_k_cyan_free_bound      0.0000        0.000            0.0           0.00
log_k_cyan_bound_free      0.0000        0.000            0.0           0.00
log_k_JCZ38                0.0000        0.000            0.0           0.00
log_k_J9Z38                0.0000        0.000            0.0           0.00
log_k_JSE76                0.0000        0.000            0.0           0.00
f_cyan_ilr_1               0.6349        0.000            0.0           0.00
f_cyan_ilr_2               0.0000        1.797            0.0           0.00
f_JCZ38_qlogis             0.0000        0.000           15.6           0.00
f_JSE76_qlogis             0.0000        0.000            0.0          17.52

Starting values for error model parameters:
a.1
  1
```

```
Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2280 2272  -1120

Optimised parameters:
                             est.   lower  upper
cyan_free_0               102.6532      NA     NA
log_k_cyan_free            -2.8547      NA     NA
log_k_cyan_free_bound      -2.7004      NA     NA
log_k_cyan_bound_free      -3.5078      NA     NA
log_k_JCZ38                -2.9255      NA     NA
log_k_J9Z38                -5.1089      NA     NA
log_k_JSE76                -3.6263      NA     NA
f_cyan_ilr_1                0.6873      NA     NA
f_cyan_ilr_2                0.6498      NA     NA
f_JCZ38_qlogis           3624.2149      NA     NA
f_JSE76_qlogis              1.9991      NA     NA
a.1                         2.7472 2.55559 2.9388
SD.log_k_cyan_free          0.3227 0.10296 0.5423
SD.log_k_cyan_free_bound    0.8757 0.29525 1.4562
SD.log_k_cyan_bound_free    0.6128 0.20220 1.0233
SD.log_k_JCZ38              1.3431 0.48474 2.2014
SD.log_k_J9Z38              0.6881 0.14714 1.2291
SD.log_k_JSE76              0.6461 0.15321 1.1390
SD.f_cyan_ilr_1             0.3361 0.11376 0.5585
SD.f_cyan_ilr_2             0.4286 0.08419 0.7730

Correlation is not available

Random effects:
                           est.   lower  upper
SD.log_k_cyan_free       0.3227 0.10296 0.5423
SD.log_k_cyan_free_bound 0.8757 0.29525 1.4562
SD.log_k_cyan_bound_free 0.6128 0.20220 1.0233
SD.log_k_JCZ38           1.3431 0.48474 2.2014
SD.log_k_J9Z38           0.6881 0.14714 1.2291
SD.log_k_JSE76           0.6461 0.15321 1.1390
SD.f_cyan_ilr_1          0.3361 0.11376 0.5585
SD.f_cyan_ilr_2          0.4286 0.08419 0.7730

Variance model:
     est. lower upper
a.1 2.747 2.556 2.939

Backtransformed parameters:
                         est. lower upper
cyan_free_0          1.027e+02    NA    NA
k_cyan_free          5.758e-02    NA    NA
k_cyan_free_bound    6.718e-02    NA    NA
k_cyan_bound_free    2.996e-02    NA    NA
k_JCZ38              5.364e-02    NA    NA
k_J9Z38              6.042e-03    NA    NA
k_JSE76              2.662e-02    NA    NA
f_cyan_free_to_JCZ38 6.039e-01    NA    NA
f_cyan_free_to_J9Z38 2.285e-01    NA    NA
f_JCZ38_to_JSE76     1.000e+00    NA    NA
f_JSE76_to_JCZ38     8.807e-01    NA    NA

Estimated Eigenvalues of SFORB model(s):
cyan_b1 cyan_b2  cyan_g
 0.1426  0.0121  0.3484

Resulting formation fractions:
                     ff
cyan_free_JCZ38 0.6039
cyan_free_J9Z38 0.2285
cyan_free_sink  0.1676
cyan_free       1.0000
JCZ38_JSE76     1.0000
JCZ38_sink      0.0000
JSE76_JCZ38     0.8807
JSE76_sink      0.1193

Estimated disappearance times:
        DT50   DT90 DT50back DT50_cyan_b1 DT50_cyan_b2
cyan   23.84 154.95    46.65         4.86        57.31
JCZ38  12.92  42.93       NA           NA           NA
J9Z38 114.71 381.07       NA           NA           NA
JSE76  26.04  86.51       NA           NA           NA
```

Listing 19: Hierarchical SFORB path 2 fit with reduced random effects, two-component error

```
saemix version used for fitting:      3.3
mkin version used for pre-fitting:  1.2.9
R version used for fitting:         4.4.2
Date of fit:     Thu Feb 13 19:05:33 2025
Date of summary: Thu Feb 13 19:05:54 2025

Equations:
d_cyan_free/dt = - k_cyan_free * cyan_free - k_cyan_free_bound *
          cyan_free + k_cyan_bound_free * cyan_bound
d_cyan_bound/dt = + k_cyan_free_bound * cyan_free - k_cyan_bound_free *
          cyan_bound
d_JCZ38/dt = + f_cyan_free_to_JCZ38 * k_cyan_free * cyan_free - k_JCZ38
          * JCZ38 + f_JSE76_to_JCZ38 * k_JSE76 * JSE76
d_J9Z38/dt = + f_cyan_free_to_J9Z38 * k_cyan_free * cyan_free - k_J9Z38
          * J9Z38
d_JSE76/dt = + f_JCZ38_to_JSE76 * k_JCZ38 * JCZ38 - k_JSE76 * JSE76

Data:
433 observations of 4 variable(s) grouped in 5 datasets

Model predictions using solution type deSolve

Fitted in 940.602 s
Using 300, 100 iterations and 10 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
          cyan_free_0       log_k_cyan_free log_k_cyan_free_bound
            101.7511               -2.8370               -3.0162
log_k_cyan_bound_free           log_k_JCZ38           log_k_J9Z38
             -3.6600               -2.2988               -5.3129
          log_k_JSE76          f_cyan_ilr_1          f_cyan_ilr_2
             -3.6991                0.6722                4.8596
       f_JCZ38_qlogis        f_JSE76_qlogis
              13.4678               14.2149

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                     cyan_free_0 log_k_cyan_free log_k_cyan_free_bound
cyan_free_0                5.629           0.000                 0.000
log_k_cyan_free            0.000           0.446                 0.000
log_k_cyan_free_bound      0.000           0.000                 1.449
log_k_cyan_bound_free      0.000           0.000                 0.000
log_k_JCZ38                0.000           0.000                 0.000
log_k_J9Z38                0.000           0.000                 0.000
log_k_JSE76                0.000           0.000                 0.000
f_cyan_ilr_1               0.000           0.000                 0.000
f_cyan_ilr_2               0.000           0.000                 0.000
f_JCZ38_qlogis             0.000           0.000                 0.000
f_JSE76_qlogis             0.000           0.000                 0.000
                     log_k_cyan_bound_free log_k_JCZ38 log_k_J9Z38 log_k_JSE76
cyan_free_0                          0.000      0.0000       0.000      0.0000
log_k_cyan_free                      0.000      0.0000       0.000      0.0000
log_k_cyan_free_bound                0.000      0.0000       0.000      0.0000
log_k_cyan_bound_free                1.213      0.0000       0.000      0.0000
log_k_JCZ38                          0.000      0.7801       0.000      0.0000
log_k_J9Z38                          0.000      0.0000       1.575      0.0000
log_k_JSE76                          0.000      0.0000       0.000      0.8078
f_cyan_ilr_1                         0.000      0.0000       0.000      0.0000
f_cyan_ilr_2                         0.000      0.0000       0.000      0.0000
f_JCZ38_qlogis                       0.000      0.0000       0.000      0.0000
f_JSE76_qlogis                       0.000      0.0000       0.000      0.0000
                     f_cyan_ilr_1 f_cyan_ilr_2 f_JCZ38_qlogis f_JSE76_qlogis
cyan_free_0                0.0000        0.000           0.00           0.00
log_k_cyan_free            0.0000        0.000           0.00           0.00
log_k_cyan_free_bound      0.0000        0.000           0.00           0.00
log_k_cyan_bound_free      0.0000        0.000           0.00           0.00
log_k_JCZ38                0.0000        0.000           0.00           0.00
log_k_J9Z38                0.0000        0.000           0.00           0.00
log_k_JSE76                0.0000        0.000           0.00           0.00
f_cyan_ilr_1               0.6518        0.000           0.00           0.00
f_cyan_ilr_2               0.0000        9.981           0.00           0.00
f_JCZ38_qlogis             0.0000        0.000          14.26           0.00
f_JSE76_qlogis             0.0000        0.000           0.00          16.17

Starting values for error model parameters:
a.1 b.1
  1   1
```

```
Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  2241 2233  -1101

Optimised parameters:
                             est.   lower   upper
cyan_free_0              100.95469      NA      NA
log_k_cyan_free           -3.18706      NA      NA
log_k_cyan_free_bound     -3.38455      NA      NA
log_k_cyan_bound_free     -3.75788      NA      NA
log_k_JCZ38               -2.77024      NA      NA
log_k_J9Z38               -5.03665      NA      NA
log_k_JSE76               -3.60289      NA      NA
f_cyan_ilr_1               0.72263      NA      NA
f_cyan_ilr_2               1.45352      NA      NA
f_JCZ38_qlogis             2.00778      NA      NA
f_JSE76_qlogis           941.58570      NA      NA
a.1                        2.11130 1.91479 2.30780
b.1                        0.06299 0.05152 0.07445
SD.log_k_cyan_free         0.50098 0.18805 0.81390
SD.log_k_cyan_bound_free   0.31671 0.08467 0.54875
SD.log_k_JCZ38             1.25865 0.45932 2.05798
SD.log_k_J9Z38             0.86833 0.27222 1.46444
SD.log_k_JSE76             0.59325 0.14711 1.03940
SD.f_cyan_ilr_1            0.35705 0.12521 0.58890
SD.f_cyan_ilr_2            0.88541 0.13797 1.63286

Correlation is not available

Random effects:
                            est.   lower  upper
SD.log_k_cyan_free       0.5010 0.18805 0.8139
SD.log_k_cyan_bound_free 0.3167 0.08467 0.5487
SD.log_k_JCZ38           1.2587 0.45932 2.0580
SD.log_k_J9Z38           0.8683 0.27222 1.4644
SD.log_k_JSE76           0.5933 0.14711 1.0394
SD.f_cyan_ilr_1          0.3571 0.12521 0.5889
SD.f_cyan_ilr_2          0.8854 0.13797 1.6329

Variance model:
       est.   lower   upper
a.1 2.11130 1.91479 2.30780
b.1 0.06299 0.05152 0.07445

Backtransformed parameters:
                         est. lower upper
cyan_free_0          1.010e+02    NA    NA
k_cyan_free          4.129e-02    NA    NA
k_cyan_free_bound    3.389e-02    NA    NA
k_cyan_bound_free    2.333e-02    NA    NA
k_JCZ38              6.265e-02    NA    NA
k_J9Z38              6.495e-03    NA    NA
k_JSE76              2.724e-02    NA    NA
f_cyan_free_to_JCZ38 6.844e-01    NA    NA
f_cyan_free_to_J9Z38 2.463e-01    NA    NA
f_JCZ38_to_JSE76     8.816e-01    NA    NA
f_JSE76_to_JCZ38     1.000e+00    NA    NA

Estimated Eigenvalues of SFORB model(s):
cyan_b1 cyan_b2  cyan_g
0.08751 0.01101 0.39586

Resulting formation fractions:
                      ff
cyan_free_JCZ38 0.68444
cyan_free_J9Z38 0.24633
cyan_free_sink  0.06923
cyan_free       1.00000
JCZ38_JSE76     0.88161
JCZ38_sink      0.11839
JSE76_JCZ38     1.00000
JSE76_sink      0.00000

Estimated disappearance times:
        DT50   DT90 DT50back DT50_cyan_b1 DT50_cyan_b2
cyan   25.36 163.36    49.18        7.921        62.95
JCZ38  11.06  36.75       NA           NA           NA
J9Z38 106.71 354.49       NA           NA           NA
JSE76  25.44  84.51       NA           NA           NA
```

Session info

```
R version 4.4.2 (2024-10-31)
Platform: x86_64-pc-linux-gnu
Running under: Debian GNU/Linux 12 (bookworm)

Matrix products: default
BLAS:   /usr/lib/x86_64-linux-gnu/blas/libblas.so.3.11.0
LAPACK: /usr/lib/x86_64-linux-gnu/lapack/liblapack.so.3.11.0

locale:
 [1] LC_CTYPE=de_DE.UTF-8       LC_NUMERIC=C
 [3] LC_TIME=de_DE.UTF-8        LC_COLLATE=de_DE.UTF-8
 [5] LC_MONETARY=de_DE.UTF-8    LC_MESSAGES=de_DE.UTF-8
 [7] LC_PAPER=de_DE.UTF-8       LC_NAME=C
 [9] LC_ADDRESS=C               LC_TELEPHONE=C
[11] LC_MEASUREMENT=de_DE.UTF-8 LC_IDENTIFICATION=C

time zone: Europe/Berlin
tzcode source: system (glibc)

attached base packages:
[1] parallel  stats     graphics  grDevices utils     datasets  methods
[8] base

other attached packages:
[1] saemix_3.3      npde_3.5        knitr_1.49      mkin_1.2.9
[5] rmarkdown_2.29  nvimcom_0.9-167

loaded via a namespace (and not attached):
 [1] gtable_0.3.6      dplyr_1.1.4       compiler_4.4.2    tinytex_0.54
 [5] tidyselect_1.2.1  colorout_1.3-2    gridExtra_2.3     callr_3.7.6
 [9] scales_1.3.0      yaml_2.3.10       fastmap_1.2.0     readxl_1.4.3
[13] lattice_0.22-6    ggplot2_3.5.1     R6_2.5.1          generics_0.1.3
[17] lmtest_0.9-40     MASS_7.3-61       tibble_3.2.1      munsell_0.5.1
[21] pillar_1.9.0      rlang_1.1.4       utf8_1.2.4        deSolve_1.40
[25] inline_0.3.20     xfun_0.49         cli_3.6.3         magrittr_2.0.3
[29] ps_1.8.1          processx_3.8.4    digest_0.6.37     grid_4.4.2
[33] mclust_6.1.1      lifecycle_1.0.4   nlme_3.1-166      vctrs_0.6.5
[37] evaluate_1.0.1    glue_1.8.0        cellranger_1.1.0  codetools_0.2-20
[41] zoo_1.8-12        pkgbuild_1.4.5    fansi_1.0.6       colorspace_2.1-1
[45] tools_4.4.2       pkgconfig_2.0.3   htmltools_0.5.8.1
```

Hardware info

```
CPU model: AMD Ryzen 9 7950X 16-Core Processor

MemTotal:       64927788 kB
```