

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 | 2 |
| Test data | 3 |
| Parent only evaluations | 9 |
| Pathway fits | 10 |
| Evaluations with pathway established previously | 10 |
| Alternative pathway fits | 15 |
| Refinement of alternative pathway fits | 21 |
| Conclusion | 23 |
| Acknowledgements | 23 |
| Appendix | 24 |
| Plots of fits that were not refined further | 24 |
| Hierarchical fit listings | 27 |
| Pathway 1 | 27 |
| Pathway 2 | 45 |
| Pathway 2, refined fits | 59 |
| Session info | 69 |
| Hardware info | 69 |

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 `mkim` package. Residue data and time step normalisation factors are read in using the function `read_spreadsheet` from the `mkim` package. This function also performs the time step normalisation.

```
data_file <- system.file(  
  "testdata", "cyantraniliprole_soil_efsa_2014.xlsx",  
  package = "mkim")  
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 obtained with the FOMC model, followed by SFORB and DFOP.

```
stopCluster(c1)
```

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("SF0", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SF0", "JSE76"),
    J9Z38 = mkinsub("SF0"),
    JSE76 = mkinsub("SF0"), quiet = TRUE,
    name = "sfo_path_1", dll_dir = "cyan_dlls", overwrite = TRUE),
  fomc_path_1 = mkinmod(
    cyan = mkinsub("FOMC", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SF0", "JSE76"),
    J9Z38 = mkinsub("SF0"),
    JSE76 = mkinsub("SF0"), quiet = TRUE,
    name = "fomc_path_1", dll_dir = "cyan_dlls", overwrite = TRUE),
  dfop_path_1 = mkinmod(
    cyan = mkinsub("DFOP", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SF0", "JSE76"),
    J9Z38 = mkinsub("SF0"),
    JSE76 = mkinsub("SF0"), quiet = TRUE,
    name = "dfop_path_1", dll_dir = "cyan_dlls", overwrite = TRUE),
  sforb_path_1 = mkinmod(
    cyan = mkinsub("SFORB", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SF0", "JSE76"),
    J9Z38 = mkinsub("SF0"),
    JSE76 = mkinsub("SF0"), quiet = TRUE,
    name = "sforb_path_1", dll_dir = "cyan_dlls", overwrite = TRUE),
  hs_path_1 = mkinmod(
    cyan = mkinsub("HS", c("JCZ38", "J9Z38")),
    JCZ38 = mkinsub("SF0", "JSE76"),
    J9Z38 = mkinsub("SF0"),
    JSE76 = mkinsub("SF0"), 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 `mkim` 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 (θ) and the random effects (Ω), 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"]])
```

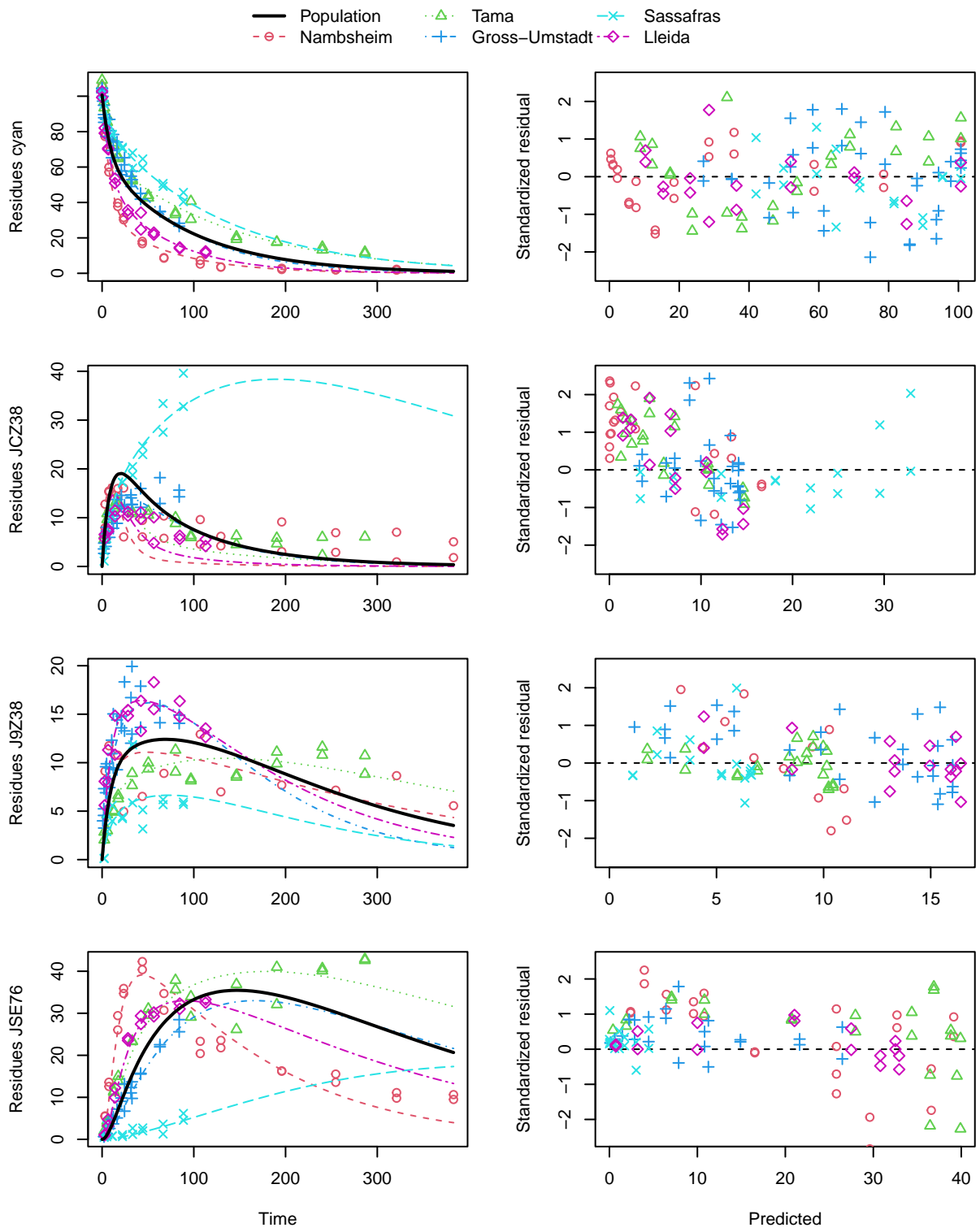


Figure 1: DFOP pathway fit with two-component error

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

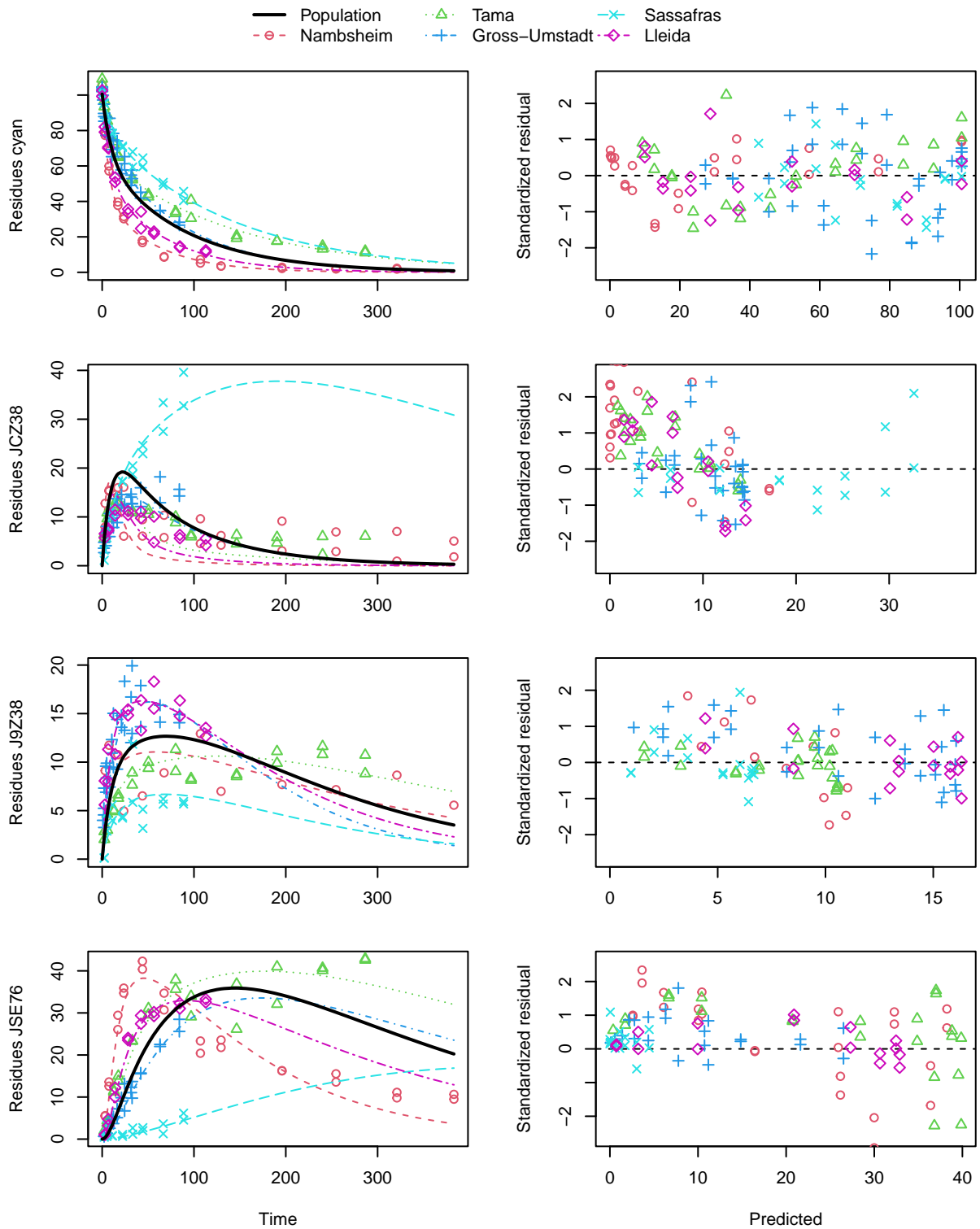


Figure 2: SFORB pathway fit with two-component error

A closer graphical analysis of these Figures shows that the residues of transformation product JCZ38 in the soils Tama and Nambshheim 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("SF0", "JSE76"),  
    J9Z38 = mkinsub("SF0"),  
    JSE76 = mkinsub("SF0", "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("SF0", "JSE76"),  
    J9Z38 = mkinsub("SF0"),  
    JSE76 = mkinsub("SF0", "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("SF0", "JSE76"),  
    J9Z38 = mkinsub("SF0"),  
    JSE76 = mkinsub("SF0", "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"]])
```

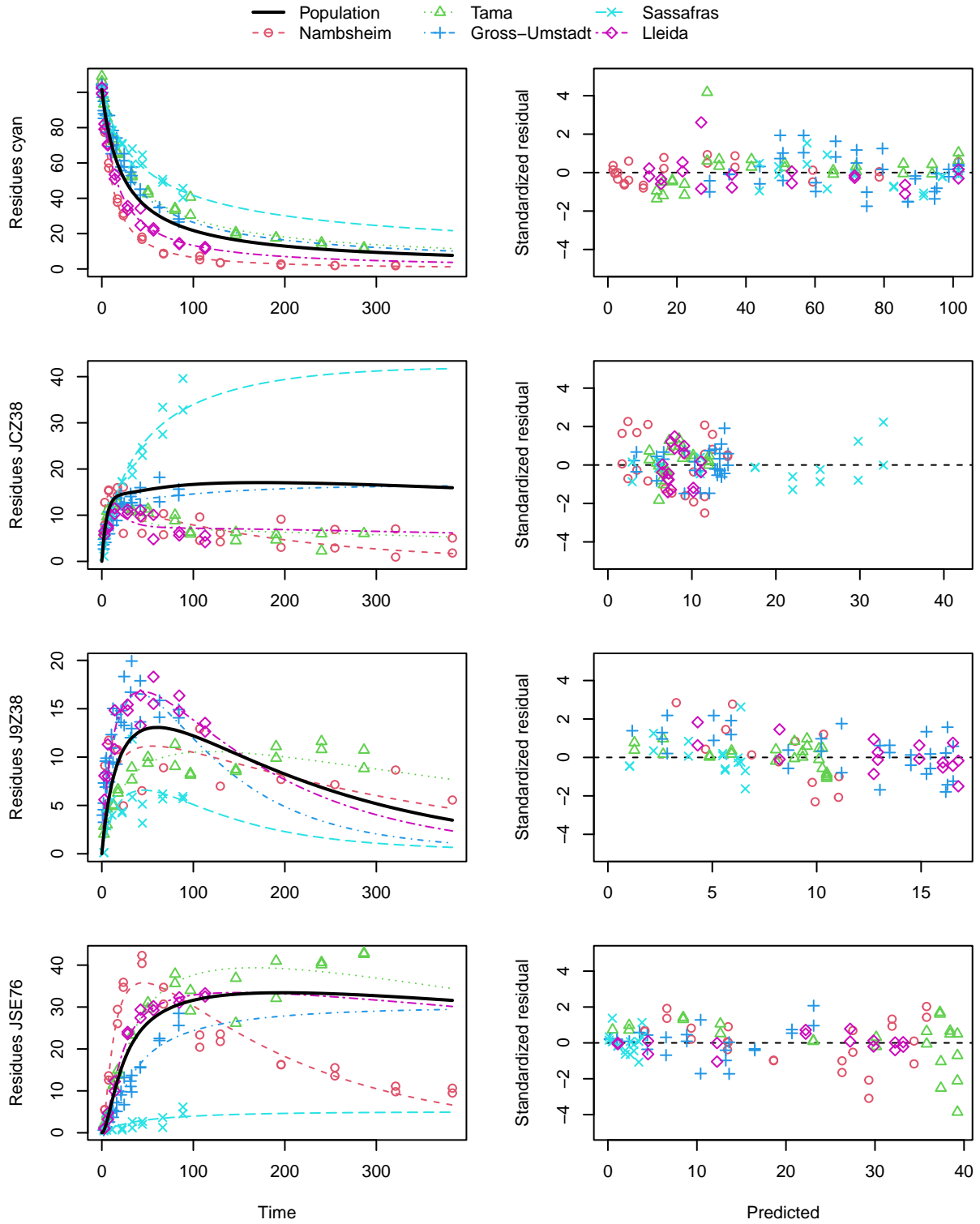


Figure 3: FOMC pathway fit with two-component error, alternative pathway

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

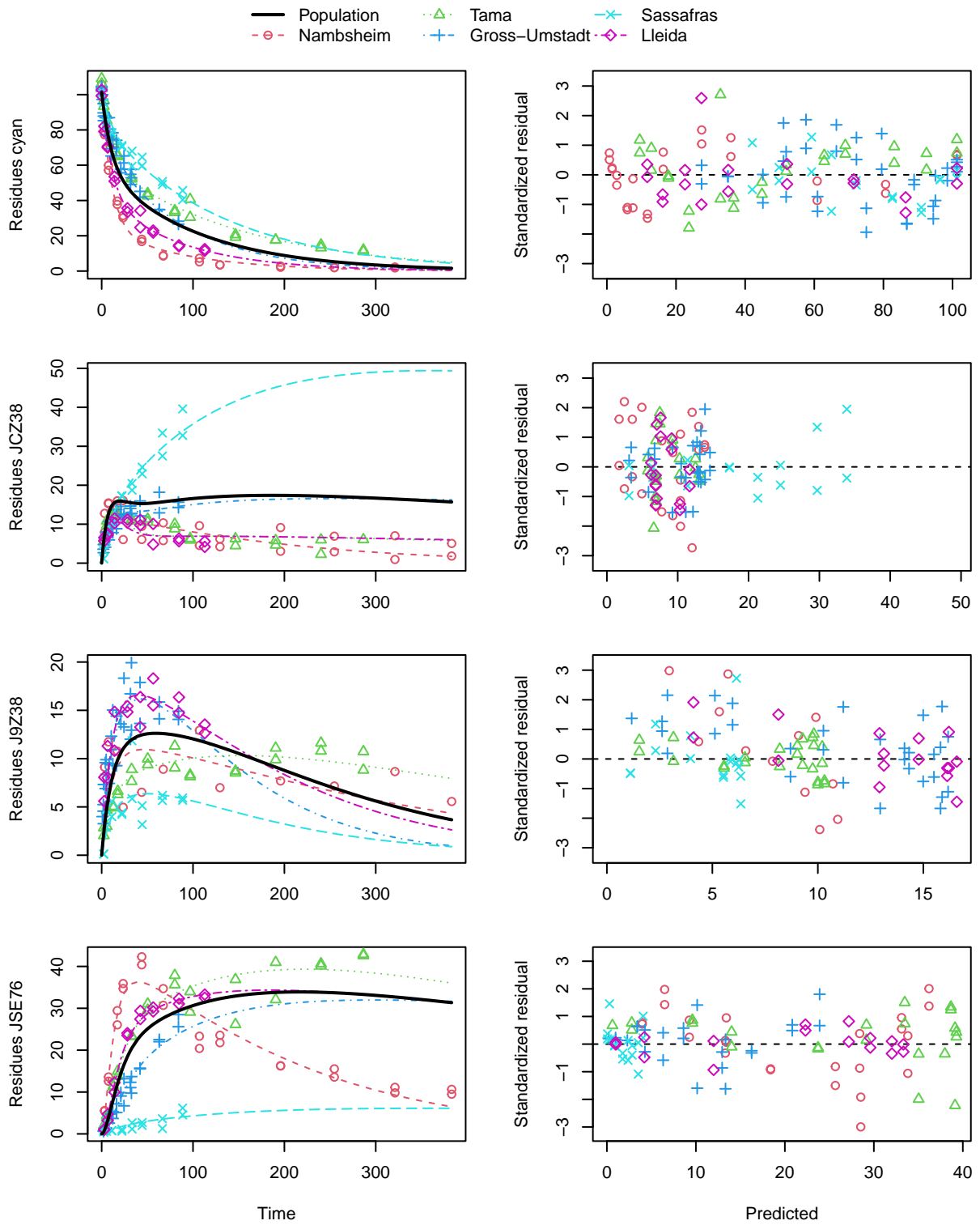


Figure 4: DFOP pathway fit with two-component error, alternative pathway

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

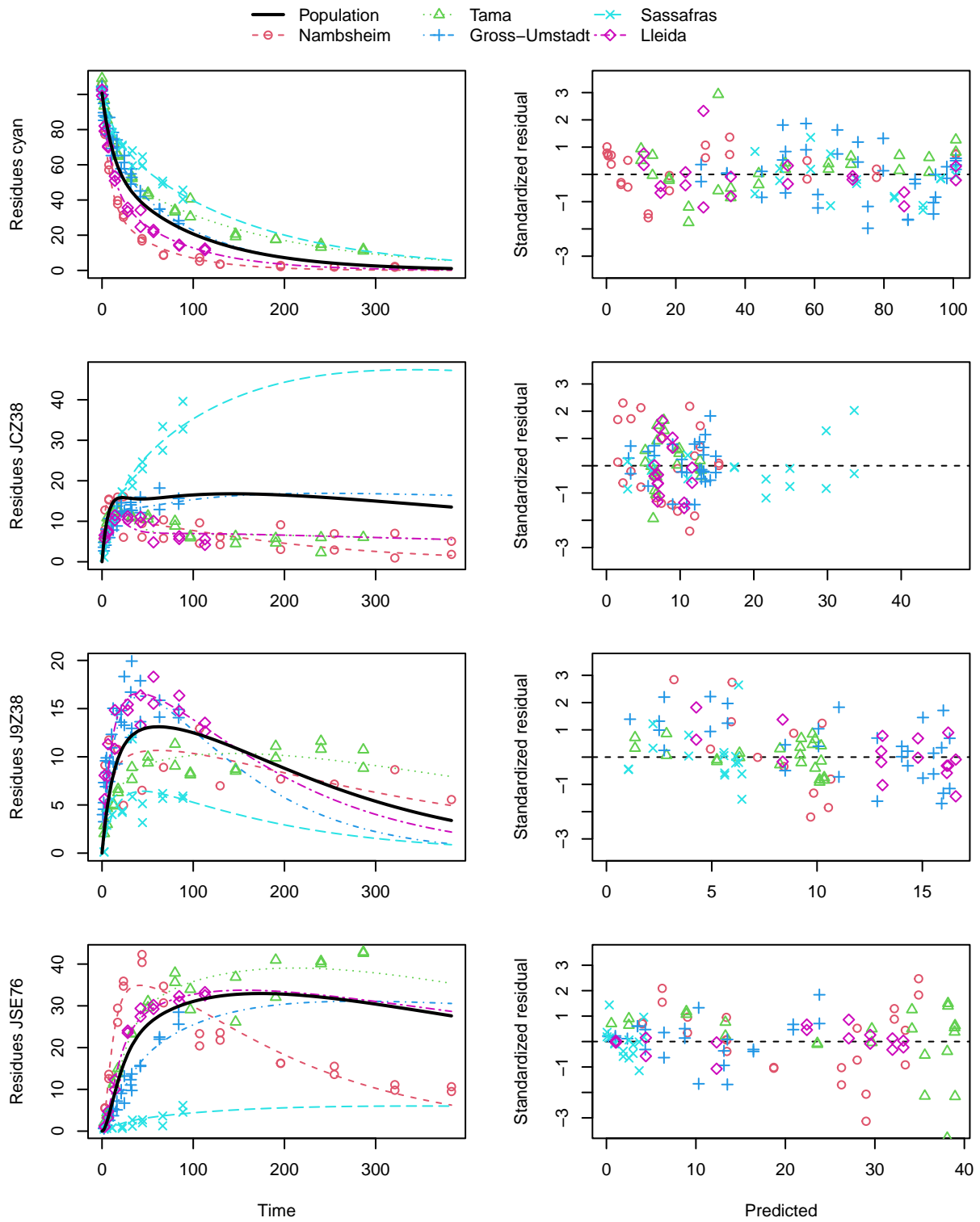


Figure 5: SFORB pathway fit with two-component error, alternative pathway

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"]])
```

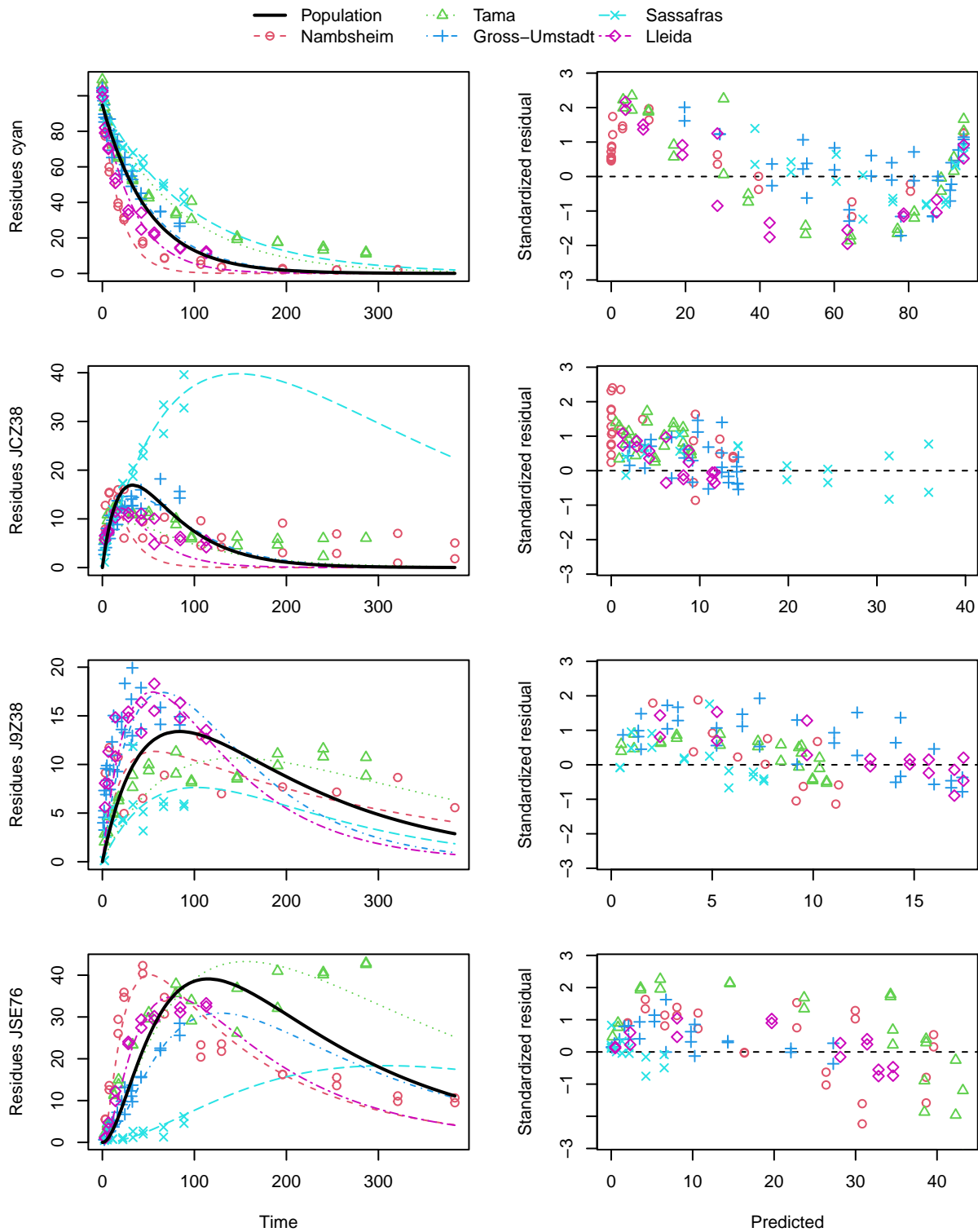


Figure 6: SFO pathway fit with two-component error


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

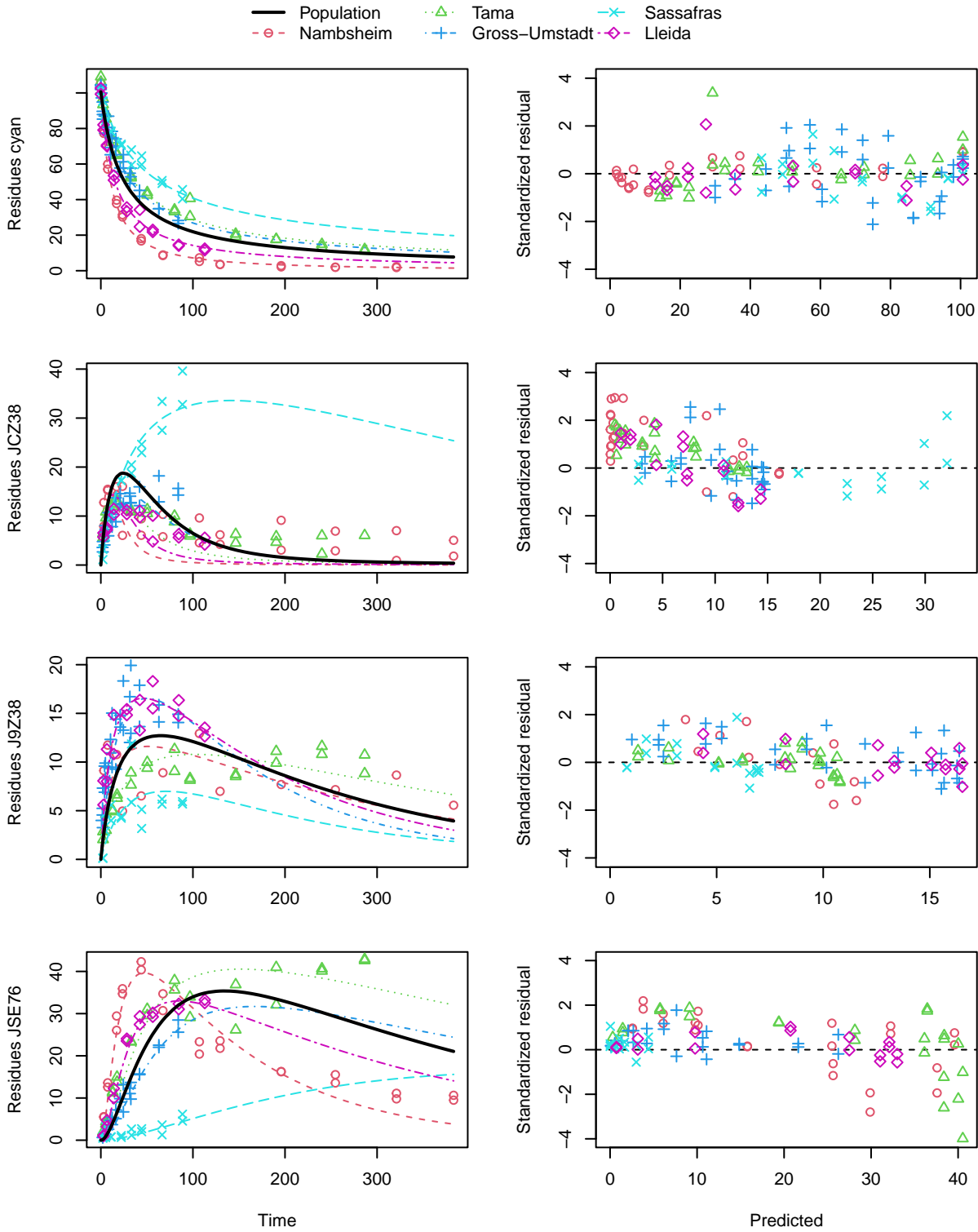


Figure 7: FOMC pathway fit with two-component error

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

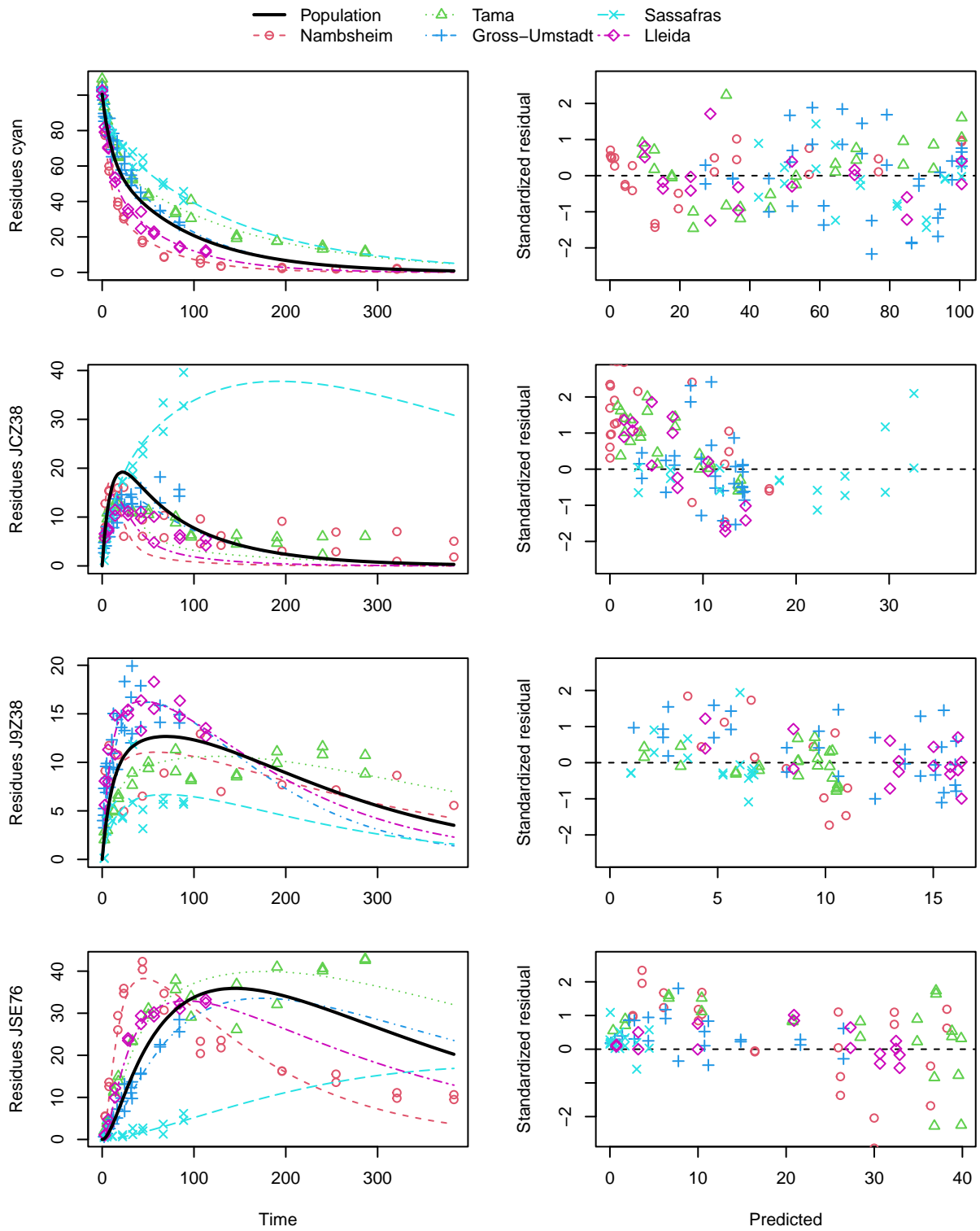


Figure 8: HS pathway fit with two-component error

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
4.797 0.0000 0.000 0.000 0.000 0.0000
log_k_cyan 0.000 0.9619 0.000 0.000 0.000 0.0000
log_k_JCZ38 0.000 0.0000 2.139 0.000 0.000 0.0000
log_k_J9Z38 0.000 0.0000 0.000 0.000 1.639 0.0000
log_k_JSE76 0.000 0.0000 0.000 0.000 0.000 0.7894
f_cyan_ilr_1 0.000 0.0000 0.000 0.000 0.000 0.0000
f_cyan_ilr_2 0.000 0.0000 0.000 0.000 0.000 0.0000
f_JCZ38_qlogis 0.000 0.0000 0.000 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 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      cyan_0      log_k_JCZ38      log_k_J9Z38      log_k_JSE76      f_cyan_ilr_1
5.416       0.000       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
5.649      0.000      0.000      0.000      0.000      0.0000
log_k_JCZ38 0.000      2.319      0.000      0.000      0.0000
log_k_J9Z38 0.000      0.000      1.73      0.000      0.0000
log_k_JSE76 0.000      0.000      0.000      1.86      0.0000
f_cyan_ilr_1 0.000      0.000      0.000      0.000      0.7183
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_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  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 0.00      12.85      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  0.00  0.0000  0.0000  0.000
log_k_JCZ38 0.00      0.00  0.00  0.0000  0.0000  0.000
log_k_J9Z38 0.00      0.00  0.00  0.0000  0.0000  0.000
log_k_JSE76 0.00      0.00  0.00  0.0000  0.0000  0.000
f_cyan_ilr_1 0.00      0.00  0.00  0.0000  0.0000  0.000
f_cyan_ilr_2 0.00      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
5.317  0.000  0.000  0.000  0.000  0.0000
log_k_JCZ38  0.000  2.272  0.000  0.000  0.000  0.0000
log_k_J9Z38  0.000  0.000  1.633  0.000  0.000  0.0000
log_k_JSE76  0.000  0.000  0.000  1.271  0.000  0.0000
f_cyan_ilr_1  0.000  0.000  0.000  0.000  0.000  0.6839
f_cyan_ilr_2  0.000  0.000  0.000  0.000  0.000  0.0000
f_JCZ38_qlogis  0.000  0.000  0.000  0.000  0.000  0.0000
log_k1  0.000  0.000  0.000  0.000  0.000  0.0000
log_k2  0.000  0.000  0.000  0.000  0.000  0.0000
g_qlogis  0.000  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  0.00  0.0000  0.0000  0.000  0.000
log_k_JCZ38  0.00  0.00  0.00  0.0000  0.0000  0.000  0.000
log_k_J9Z38  0.00  0.00  0.00  0.0000  0.0000  0.000  0.000
log_k_JSE76  0.00  0.00  0.00  0.0000  0.0000  0.000  0.000
f_cyan_ilr_1  0.00  0.00  0.00  0.0000  0.0000  0.000  0.000
f_cyan_ilr_2  11.95  0.00  0.00  0.0000  0.0000  0.000  0.000
f_JCZ38_qlogis  0.00  16.08  0.0000  0.0000  0.000  0.000
log_k1  0.00  0.00  0.9496  0.0000  0.000  0.000
log_k2  0.00  0.00  0.00  0.0000  0.5846  0.000  0.000
g_qlogis  0.00  0.00  0.00  0.0000  0.0000  1.719  0.000

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
4.466            0.0000            0.000
log_k_cyan_free  0.000            0.6158            0.000
log_k_cyan_bound_free      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_bound_free      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_bound_free      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
5.317            0.0000          0.000
log_k_cyan_free  0.000            0.7301          0.000
log_k_cyan_bound_free  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_bound_free  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_bound_free  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 0.000 0.0000
log_k_JCZ38 0.000 1.448 0.000 0.000 0.000 0.0000
log_k_J9Z38 0.000 0.000 1.724 0.000 0.000 0.0000
log_k_JSE76 0.000 0.000 0.000 3.659 0.000 0.0000
f_cyan_ilr_1 0.000 0.000 0.000 0.000 0.000 0.6356
f_cyan_ilr_2 0.000 0.000 0.000 0.000 0.000 0.0000
f_JCZ38_qlogis 0.000 0.000 0.000 0.000 0.000 0.0000
f_JSE76_qlogis 0.000 0.000 0.000 0.000 0.000 0.0000
log_alpha 0.000 0.000 0.000 0.000 0.000 0.0000
log_beta 0.000 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 0.00 0.0000 0.0000
log_k_JCZ38 0.00 0.00 0.00 0.00 0.0000 0.0000
log_k_J9Z38 0.00 0.00 0.00 0.00 0.0000 0.0000
log_k_JSE76 0.00 0.00 0.00 0.00 0.0000 0.0000
f_cyan_ilr_1 0.00 0.00 0.00 0.00 0.0000 0.0000
f_cyan_ilr_2 10.32 0.00 0.00 0.00 0.0000 0.0000
f_JCZ38_qlogis 0.00 12.23 0.00 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 | 1__JCZ3 | 1__J9Z3 | 1__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
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          0.00          0.0000 0.0000
log_k_JCZ38 0.000          0.00          0.00          0.00          0.0000 0.0000
log_k_J9Z38 0.000          0.00          0.00          0.00          0.0000 0.0000
log_k_JSE76 0.000          0.00          0.00          0.00          0.0000 0.0000
f_cyan_ilr_1 0.000          0.00          0.00          0.00          0.0000 0.0000
f_cyan_ilr_2 1.797          0.00          0.00          0.00          0.0000 0.0000
f_JCZ38_qlogis 0.000          13.86         0.00          0.00          0.0000 0.0000
f_JSE76_qlogis 0.000          0.00          13.91         0.00          0.0000 0.0000
log_k1       0.000          0.00          0.00          1.106         0.0000 0.0000
log_k2       0.000          0.00          0.00          0.00          0.6141 0.0000
g_qlogis     0.000          0.00          0.00          0.00          0.0000 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      0.00 0.0000 0.0000
log_k_JCZ38 0.00      0.00      0.00      0.00 0.0000 0.0000
log_k_J9Z38 0.00      0.00      0.00      0.00 0.0000 0.0000
log_k_JSE76 0.00      0.00      0.00      0.00 0.0000 0.0000
f_cyan_ilr_1 0.00      0.00      0.00      0.00 0.0000 0.0000
f_cyan_ilr_2 13.37      0.00      0.00      0.00 0.0000 0.0000
f_JCZ38_qlogis 0.00      14.21      0.00      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      0.00 0.8453 0.0000
log_k2      0.00      0.00      0.00      0.00 0.0000 0.5969
g_qlogis    0.00      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
4.589            0.0000          0.0000
log_k_cyan_free  0.000           0.4849          0.0000
log_k_cyan_bound_free  0.000          0.0000          1.62
log_k_cyan_bound_free  0.000          0.0000          0.0000
log_k_JCZ38      0.000           0.0000          0.0000
log_k_J9Z38      0.000           0.0000          0.0000
log_k_JSE76      0.000           0.0000          0.0000
f_cyan_ilr_1     0.000           0.0000          0.0000
f_cyan_ilr_2     0.000           0.0000          0.0000
f_JCZ38_qlogis   0.000           0.0000          0.0000
f_JSE76_qlogis   0.000           0.0000          0.0000
cyan_free_0      log_k_cyan_bound_free  log_k_JCZ38  log_k_J9Z38  log_k_JSE76
0.000           0.0000          0.0000          0.0000          0.0
log_k_cyan_free  0.000           0.0000          0.0000          0.0000          0.0
log_k_cyan_bound_free  0.000           0.0000          0.0000          0.0000          0.0
log_k_cyan_bound_free  1.197           0.0000          0.0000          0.0000          0.0
log_k_JCZ38      0.000           0.7966          0.0000          0.0000          0.0
log_k_J9Z38      0.000           0.0000          1.561           0.0000          0.0
log_k_JSE76      0.000           0.0000          0.0000          0.0000          0.8
f_cyan_ilr_1     0.000           0.0000          0.0000          0.0000          0.0
f_cyan_ilr_2     0.000           0.0000          0.0000          0.0000          0.0
f_JCZ38_qlogis   0.000           0.0000          0.0000          0.0000          0.0
f_JSE76_qlogis   0.000           0.0000          0.0000          0.0000          0.0
cyan_free_0      f_cyan_ilr_1  f_cyan_ilr_2  f_JCZ38_qlogis  f_JSE76_qlogis
0.0000          0.0000          0.0000          0.0000          0.0000
log_k_cyan_free  0.0000          0.0000          0.0000          0.0000          0.0000
log_k_cyan_bound_free  0.0000          0.0000          0.0000          0.0000          0.0000
log_k_cyan_bound_free  0.0000          0.0000          0.0000          0.0000          0.0000
log_k_JCZ38      0.0000          0.0000          0.0000          0.0000          0.0000
log_k_J9Z38      0.0000          0.0000          0.0000          0.0000          0.0000
log_k_JSE76      0.0000          0.0000          0.0000          0.0000          0.0000
f_cyan_ilr_1     0.6349          0.0000          0.0000          0.0000          0.0000
f_cyan_ilr_2     0.0000          1.797          0.0000          0.0000          0.0000
f_JCZ38_qlogis   0.0000          0.0000          15.6           0.0000          0.0000
f_JSE76_qlogis   0.0000          0.0000          0.0000          0.0000          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
5.629            0.000           0.000
log_k_cyan_free  0.000           0.446           0.000
log_k_cyan_bound_free  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
cyan_free_0      log_k_cyan_bound_free  log_k_JCZ38  log_k_J9Z38  log_k_JSE76
0.000            0.000           0.0000      0.000       0.0000
log_k_cyan_free  0.000            0.0000      0.000       0.000       0.0000
log_k_cyan_bound_free  0.000            0.0000      0.000       0.000       0.0000
log_k_cyan_bound_free  1.213            0.0000      0.000       0.000       0.0000
log_k_JCZ38      0.000            0.7801      0.000       0.000       0.0000
log_k_J9Z38      0.000            0.0000      1.575       0.000       0.0000
log_k_JSE76      0.000            0.0000      0.000       0.8078      0.0000
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_JSE76_qlogis   0.000            0.0000      0.000       0.000       0.0000
cyan_free_0      f_cyan_ilr_1  f_cyan_ilr_2  f_JCZ38_qlogis  f_JSE76_qlogis
0.0000           0.000        0.000         0.00           0.00
log_k_cyan_free  0.0000           0.000        0.00         0.00           0.00
log_k_cyan_bound_free  0.0000           0.000        0.00         0.00           0.00
log_k_cyan_bound_free  0.0000           0.000        0.00         0.00           0.00
log_k_JCZ38      0.0000           0.000        0.00         0.00           0.00
log_k_J9Z38      0.0000           0.000        0.00         0.00           0.00
log_k_JSE76      0.0000           0.000        0.00         0.00           0.00
f_cyan_ilr_1     0.6518           0.000        0.00         0.00           0.00
f_cyan_ilr_2     0.0000           9.981        0.00         0.00           0.00
f_JCZ38_qlogis   0.0000           0.000        14.26        0.00           0.00
f_JSE76_qlogis   0.0000           0.000        0.00         16.17          0.00

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 0.000 0.0000
log_k_JCZ38 0.000 1.448 0.000 0.000 0.000 0.0000
log_k_J9Z38 0.000 0.000 1.724 0.000 0.000 0.0000
log_k_JSE76 0.000 0.000 0.000 3.659 0.000 0.0000
f_cyan_ilr_1 0.000 0.000 0.000 0.000 0.000 0.6356
f_cyan_ilr_2 0.000 0.000 0.000 0.000 0.000 0.0000
f_JCZ38_qlogis 0.000 0.000 0.000 0.000 0.000 0.0000
f_JSE76_qlogis 0.000 0.000 0.000 0.000 0.000 0.0000
log_alpha 0.000 0.000 0.000 0.000 0.000 0.0000
log_beta 0.000 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 0.00 0.0000 0.0000
log_k_JCZ38 0.00 0.00 0.00 0.00 0.0000 0.0000
log_k_J9Z38 0.00 0.00 0.00 0.00 0.0000 0.0000
log_k_JSE76 0.00 0.00 0.00 0.00 0.0000 0.0000
f_cyan_ilr_1 0.00 0.00 0.00 0.00 0.0000 0.0000
f_cyan_ilr_2 10.32 0.00 0.00 0.00 0.0000 0.0000
f_JCZ38_qlogis 0.00 12.23 0.00 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    0.00 0.000 0.0000
log_k_JCZ38    0.000    0.00    0.00    0.00 0.000 0.0000
log_k_J9Z38    0.000    0.00    0.00    0.00 0.000 0.0000
log_k_JSE76    0.000    0.00    0.00    0.00 0.000 0.0000
f_cyan_ilr_1   0.000    0.00    0.00    0.00 0.000 0.0000
f_cyan_ilr_2   1.797    0.00    0.00    0.00 0.000 0.0000
f_JCZ38_qlogis 0.000    13.86    0.00    0.00 0.000 0.0000
f_JSE76_qlogis 0.000    0.00    13.91    0.00 0.000 0.0000
log_k1         0.000    0.00    0.00    1.106 0.000 0.0000
log_k2         0.000    0.00    0.00    0.000 0.6141 0.0000
g_qlogis       0.000    0.00    0.00    0.000 0.0000 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      0.00 0.0000 0.0000
log_k_JCZ38 0.00      0.00      0.00      0.00 0.0000 0.0000
log_k_J9Z38 0.00      0.00      0.00      0.00 0.0000 0.0000
log_k_JSE76 0.00      0.00      0.00      0.00 0.0000 0.0000
f_cyan_ilr_1 0.00      0.00      0.00      0.00 0.0000 0.0000
f_cyan_ilr_2 13.37      0.00      0.00      0.00 0.0000 0.0000
f_JCZ38_qlogis 0.00      14.21      0.00      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      0.00 0.8453 0.0000
log_k2      0.00      0.00      0.00      0.00 0.0000 0.5969
g_qlogis     0.00      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 | 1.30902 | 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 |

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
4.589            0.0000          0.0000
log_k_cyan_free  0.0000          0.4849          0.0000
log_k_cyan_bound_free  0.0000          0.0000          0.0000          1.62
log_k_cyan_bound_free  0.0000          0.0000          0.0000          0.00
log_k_JCZ38      0.0000          0.0000          0.0000          0.00
log_k_J9Z38      0.0000          0.0000          0.0000          0.00
log_k_JSE76      0.0000          0.0000          0.0000          0.00
f_cyan_ilr_1     0.0000          0.0000          0.0000          0.00
f_cyan_ilr_2     0.0000          0.0000          0.0000          0.00
f_JCZ38_qlogis   0.0000          0.0000          0.0000          0.00
f_JSE76_qlogis   0.0000          0.0000          0.0000          0.00
cyan_free_0      log_k_cyan_bound_free  log_k_JCZ38  log_k_J9Z38  log_k_JSE76
0.0000          0.0000          0.0000          0.0000          0.00
log_k_cyan_free  0.0000          0.0000          0.0000          0.00
log_k_cyan_bound_free  0.0000          0.0000          0.0000          0.00
log_k_cyan_bound_free  1.197          0.0000          0.0000          0.00
log_k_JCZ38      0.0000          0.7966          0.0000          0.00
log_k_J9Z38      0.0000          0.0000          1.561          0.00
log_k_JSE76      0.0000          0.0000          0.0000          0.80
f_cyan_ilr_1     0.0000          0.0000          0.0000          0.00
f_cyan_ilr_2     0.0000          0.0000          0.0000          0.00
f_JCZ38_qlogis   0.0000          0.0000          0.0000          0.00
f_JSE76_qlogis   0.0000          0.0000          0.0000          0.00
cyan_free_0      f_cyan_ilr_1  f_cyan_ilr_2  f_JCZ38_qlogis  f_JSE76_qlogis
0.0000          0.0000          0.0000          0.0000          0.00
log_k_cyan_free  0.0000          0.0000          0.0000          0.00
log_k_cyan_bound_free  0.0000          0.0000          0.0000          0.00
log_k_cyan_bound_free  0.0000          0.0000          0.0000          0.00
log_k_JCZ38      0.0000          0.0000          0.0000          0.00
log_k_J9Z38      0.0000          0.0000          0.0000          0.00
log_k_JSE76      0.0000          0.0000          0.0000          0.00
f_cyan_ilr_1     0.6349          0.0000          0.0000          0.00
f_cyan_ilr_2     0.0000          1.797          0.0000          0.00
f_JCZ38_qlogis   0.0000          0.0000          15.6          0.00
f_JSE76_qlogis   0.0000          0.0000          0.0000          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
5.629            0.000           0.000
log_k_cyan_free  0.000           0.446           0.000
log_k_cyan_bound_free  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
cyan_free_0      log_k_cyan_bound_free  log_k_JCZ38  log_k_J9Z38  log_k_JSE76
0.000           0.000           0.000           0.000           0.000
log_k_cyan_free  0.000           0.000           0.000           0.000
log_k_cyan_bound_free  0.000           0.000           0.000           0.000
log_k_cyan_bound_free  1.213           0.000           0.000           0.000
log_k_JCZ38      0.000           0.7801          0.000           0.000
log_k_J9Z38      0.000           0.000           1.575           0.000
log_k_JSE76      0.000           0.000           0.000           0.8078
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_JSE76_qlogis   0.000           0.000           0.000           0.000
cyan_free_0      f_cyan_ilr_1  f_cyan_ilr_2  f_JCZ38_qlogis  f_JSE76_qlogis
0.0000           0.0000          0.000           0.00           0.00
log_k_cyan_free  0.0000           0.000           0.00           0.00
log_k_cyan_bound_free  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