Hierarchical kinetic modelling of degradation data

Contents

Setup

```
library(mkin)
library(knitr)
library(saemix)
library(parallel)
library(readxl)
```

```
n_cores <- detectCores()

if (Sys.info()["sysname"] == "Windows") {
  cl <- makePSOCKcluster(n_cores)
} else {
  cl <- makeForkCluster(n_cores)
}
```

Introduction

This report shows hierarchical kinetic modelling for ... The data were obtained from ...

```
data_path <- system.file(
  "testdata", "lambda-cyhalothrin_soil_efsa_2014.xlsx",
  package = "mkin")
ds <- read_spreadsheet(data_path, valid_datasets = c(1:4, 7:13))
covariates <- attr(ds, "covariates")
```

The covariate data are shown below.

Table 1: Covariate data for all datasets

	pH
18 Acres	5.50
Nebraska	7.00
Marsillargues	7.30
Speyer 5 M	7.20
Am Fischteich	5.63
Löhmingen	6.45
Speyer 2.2	5.50

The datasets with the residue time series are shown in the tables below. Please refer to the spreadsheet for details like data sources, treatment of values below reporting limits and time step normalisation factors.

Table 2: Dataset 18 Acres

time	lambda	c_Ia	c_XV	u_Z	c_V
0	100.2				
0	94.8				
7	67.6		4.8	0.6	1.1
7	69.3		5.0	0.6	1.0
14	58.1		4.5	2.5	1.0
14	44.4		4.5	3.9	1.0
30	45.5		5.4	5.0	2.4
30	45.1		5.5	5.1	1.5
59	31.4	0.9	3.5	4.8	1.6
59	33.8	0.7	3.5	5.0	1.5
91	27.5	2.9	1.2	4.3	1.7
91	30.7	2.6	1.1	4.0	1.4
120	28.1	1.6	0.8	4.2	1.3
120	37.2	2.8	0.5	2.1	0.9
0	99.0				
0	97.8				
7	60.4		6.6	1.0	1.1
7	68.0		5.6	0.6	1.0
14	54.1		5.3	1.5	1.0
14	51.1		5.6	1.7	1.0
29	47.1		3.5	3.8	2.4
29	40.3		3.1	4.4	1.5
60	34.3	0.9	3.1	4.2	1.6
60	35.3	0.7	2.9	5.0	1.5
90	32.8	2.9	2.3	3.4	1.7
90	26.8	2.6	2.1	4.0	1.4
120	17.2	1.6	1.4	2.1	1.3
120	30.4	2.8	1.7	4.3	0.9

Table 3: Dataset Nebraska

time	lambda	c_Ia	c_XV	u_Z	c_V
0	99.8				
0	98.0				
7	61.8		6.5	0.3	0.6
7	62.9		5.9	0.6	0.9
14	48.9		3.9	3.9	1.0
14	53.0		4.2	2.8	0.8
30	41.5		5.0	3.4	1.3
30	40.3		4.9	3.6	1.2
59	28.9		2.5	3.2	1.0
59	32.6		2.4	4.7	0.9
91	22.4	1.6	1.1	3.6	1.0
91	14.4	1.7	0.9	2.2	1.0
120	11.8	0.9	0.7	1.1	1.4
120	11.4	0.9	0.7	1.2	1.0
0	92.5				
0	93.4				
7	68.0		5.1	0.7	0.6
7	64.3		5.2	0.8	0.9
14	52.8		3.4	2.6	1.0
14	56.6		4.5	2.0	0.8
29	44.6		3.1	4.0	1.3
29	44.2		3.0	3.4	1.2
60	29.6		2.1	3.9	1.0
60	28.1		2.7	3.5	0.9
90	18.3	1.6	1.4	3.0	1.0
90	19.6	1.7	1.5	3.0	1.0
120	24.4	0.9	0.8	2.9	1.4
120	16.5	0.9	1.3	3.1	1.0

Table 4: Dataset Marsillargues

time	lambda	c_Ia	c_XV	u_Z	c_V
0	94.1				
0	98.3				
7	67.2		3.2	3.3	3.7
7	72.8		2.5	0.5	4.1
14	52.1		7.8	3.7	3.0
14	49.0		7.6	3.8	2.3
30	34.9	0.8	6.4	3.4	1.4
30	37.0	0.4	5.1	5.9	1.9
59	21.8		3.7	1.7	1.4
59	26.0		3.7	0.8	1.5
91	12.9	2.3	1.0	1.4	0.8
91	11.5	2.0	1.0	1.6	0.9
120	9.0	1.0	0.6	0.3	
120	9.1	1.1	0.7	0.6	
0	95.4				
0	101.7				
7	61.1		2.1	1.2	3.7
7	66.6		1.9	1.1	4.1
14	48.2		2.8	1.8	3.0
14	48.6		2.7	2.0	2.3
29	37.0	0.8	2.7	1.0	1.4
29	44.0	0.4	1.7	1.2	1.9
60	22.1		3.3	2.6	1.4
60	20.6		3.1	1.7	1.5
90	11.1	2.3	1.9	1.2	0.8
90	11.3	2.0	1.8	1.1	0.9
120	9.7	1.0	1.1	0.4	
120	10.8	1.1	1.1	0.3	

Table 5: Dataset Speyer 5 M

time	lambda	c_V	c_XV	c_Ia
0	98.9	1.10		1.0
0	100.0	1.00		1.1
7	82.4	4.10		7.8
7	88.3	4.40		8.3
14	59.0	6.10		10.9
14	55.8	5.50		15.7
28	48.7	4.40	0.25	11.7
28	62.7	8.10	0.25	12.1
56	30.3	1.80	2.10	12.4
56	47.0	2.70	0.90	1.6
90	15.3	0.25	1.80	29.7
90	17.6	0.70	1.40	16.1
120	24.7	1.00	1.70	21.8
120	19.6	1.10	1.60	15.2
0	100.9	1.10		1.0
0	100.1	1.00		1.1
7	80.4	4.10	2.10	7.8
7	80.8	4.40	2.20	8.3
14	62.6	6.10		10.9
14	61.5	5.50		15.7
28	53.4	4.40	0.25	11.7
28	55.3	8.10	0.25	12.1
56	40.6	1.80	3.00	12.4
56	33.9	2.70	0.80	1.6
90	40.4	0.25	1.50	29.7
90	38.4	0.70	1.40	16.1
120	35.8	1.00	1.40	21.8
120	32.8	1.10	1.50	15.2

Table 6: Dataset Am Fischteich

time	lambda	c_V
0	99.4	1.00
0	100.0	1.30
7	82.4	5.40
7	77.4	1.80
14	61.4	2.90
14	62.0	8.30
28	57.1	2.50
28	56.0	0.25
56	49.6	3.30
56	52.2	2.90
90	49.4	2.40
90	49.1	2.10
120	50.1	2.10
120	44.6	2.80

Table 7: Dataset Löhmingen

time	lambda	c_V	c_XV
0	98.9	1.5	
0	99.8	0.9	
7	85.5	2.1	
7	87.3	2.8	
14	70.5	1.5	
14	80.8	1.8	
28	64.2	2.7	
28	70.2	2.6	
56	72.1	3.7	
56	65.8	2.9	0.25
90	75.6	4.5	0.25
90	65.8	2.3	2.10
120	59.0	2.5	1.10
120	71.2	4.7	0.25

Table 8: Dataset Speyer 2.2

time	lambda	c_V
0	99.6	1.30
0	99.4	0.75
7	93.5	2.20
7	94.7	2.80
14	86.8	4.80
14	87.9	6.90
28	70.8	2.70
28	77.6	3.90
56	69.0	6.70
56	64.5	5.30
90	63.8	3.20
90	72.4	6.50
120	60.3	4.50
120	60.7	4.20

Parent only evaluations

The following code performs separate fits of the candidate degradation models to all datasets using constant variance and the two-component error model.

```
parent_deg_mods <- c("SFO", "FOMC", "DFOP", "SFORB")
errmods <- c(const = "constant variance", tc = "two-component error")
parent_sep_const <- mmkin(
  parent_deg_mods, ds,
  error_model = "const",
  cluster = cl, quiet = TRUE)
parent_sep_tc <- update(parent_sep_const, error_model = "tc")
```

To select the parent model, the corresponding hierarchical fits are performed below.

```
parent_mhmkin <- mhmkin(list(parent_sep_const, parent_sep_tc), cluster = cl)
status(parent_mhmkin) |> kable()
```

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

All fits terminate without errors (status OK). The check for ill-defined parameters shows that not all random effect parameters can be robustly quantified.

```
illparms(parent_mhmkin) |> kable()
```

	const	tc
SFO	sd(lambda_0)	sd(lambda_0)
FOMC	sd(lambda_0)	sd(lambda_0), b.1
DFOP	sd(lambda_0)	sd(lambda_0), b.1
SFORB	sd(lambda_free_0), sd(log_k_lambda_free_bound)	sd(lambda_free_0), sd(log_k_lambda_free_bound), b.1

Therefore, the fits are updated, excluding random effects that were ill-defined according to the `illparms` function. The status of the fits is checked.

```
parent_mhmkin_refined <- update(parent_mhmkin,
  no_random_effect = illparms(parent_mhmkin))
status(parent_mhmkin_refined) |> kable()
```

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

Also, it is checked if the AIC values of the refined fits are actually smaller than the AIC values of the original fits.

```
(AIC(parent_mhmkin_refined) < AIC(parent_mhmkin)) |> kable()
```

	const	tc
SFO	TRUE	TRUE
FOMC	TRUE	TRUE
DFOP	TRUE	TRUE
SFORB	TRUE	TRUE

From the refined fits, the most suitable model is selected using the AIC.

```
aic_parent <- AIC(parent_mhmkin_refined)
min_aic <- which(aic_parent == min(aic_parent), arr.ind = TRUE)
best_degmod_parent <- rownames(aic_parent)[min_aic[1]]
best_errmod_parent <- colnames(aic_parent)[min_aic[2]]
anova(parent_mhmkin_refined) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
SFO const	4	1177.4	1177.2	-584.7
SFO tc	5	1169.6	1169.4	-579.8
FOMC const	6	993.6	993.3	-490.8
SFORB const	7	982.7	982.3	-484.4
FOMC tc	7	995.6	995.2	-490.8
DFOP const	8	984.5	984.1	-484.2
SFORB tc	8	984.7	984.3	-484.4
DFOP tc	9	986.4	986.0	-484.2

```
parent_best <- parent_mhmkin_refined[[best_degmod_parent, best_errmod_parent]]
```

Based on the AIC, the combination of the SFORB degradation model with the error model constant variance is identified to be most suitable for the degradation of the parent. The check below confirms that no ill-defined parameters remain for this combined model.

```
illparms(parent_best)
```

The corresponding fit is plotted below.

```
plot(parent_best)
```
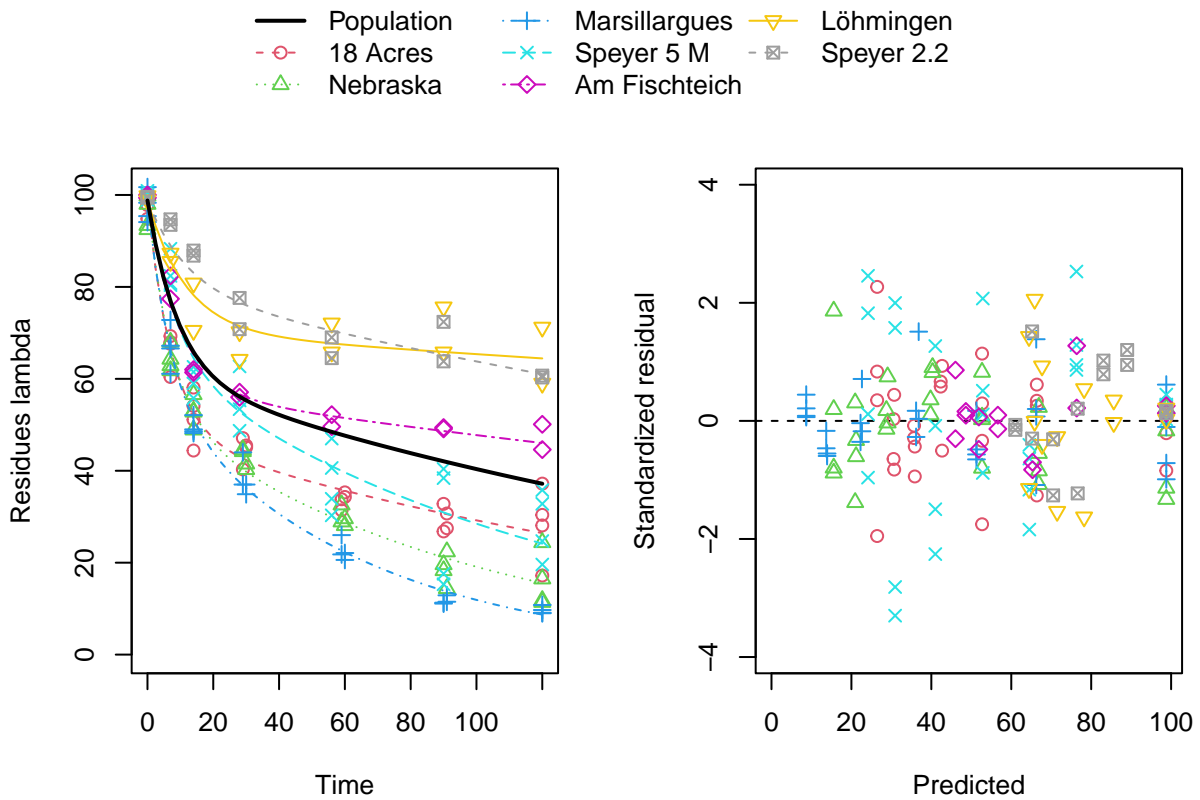
The fitted parameters, together with approximate confidence intervals are listed below.

```
parms(parent_best, ci = TRUE) |> kable(digits = 3)
```

	estimate	lower	upper
lambda_free_0	98.789	96.847	100.732
log_k_lambda_free	-3.124	-3.533	-2.715
log_k_lambda_free_bound	-2.846	-3.122	-2.570
log_k_lambda_bound_free	-4.594	-5.416	-3.772
a.1	4.739	4.185	5.294
SD.log_k_lambda_free	0.509	0.236	0.783
SD.log_k_lambda_bound_free	0.958	0.382	1.533

To investigate a potential covariate influence on degradation parameters, a covariate model is added to the hierarchical model for each of the degradation parameters with well-defined random effects. Also, a version with covariate models for both of them is fitted.

```
parent_best_pH_1 <- update(parent_best, covariates = covariates,
  covariate_models = list(log_k_lambda_free ~ pH))
parent_best_pH_2 <- update(parent_best, covariates = covariates,
  covariate_models = list(log_k_lambda_bound_free ~ pH))
parent_best_pH_3 <- update(parent_best, covariates = covariates,
  covariate_models = list(log_k_lambda_free ~ pH, log_k_lambda_bound_free ~ pH))
```

The resulting models are compared.

```
anova(parent_best, parent_best_pH_1, parent_best_pH_2, parent_best_pH_3) |>
  kable(digits = 1)
```

	npar	AIC	BIC	Lik
parent_best	7	982.7	982.3	-484.4
parent_best_pH_1	8	983.6	983.1	-483.8
parent_best_pH_2	8	981.4	981.0	-482.7
parent_best_pH_3	9	982.3	981.8	-482.2

The model fit with the lowest AIC is the one with a pH correlation of the desorption rate constant `k_lambda_bound_free`. Plot and parameter listing of this fit are shown below. Also, it is confirmed that no ill-defined variance parameters are found.

```
plot(parent_best_pH_2)
```
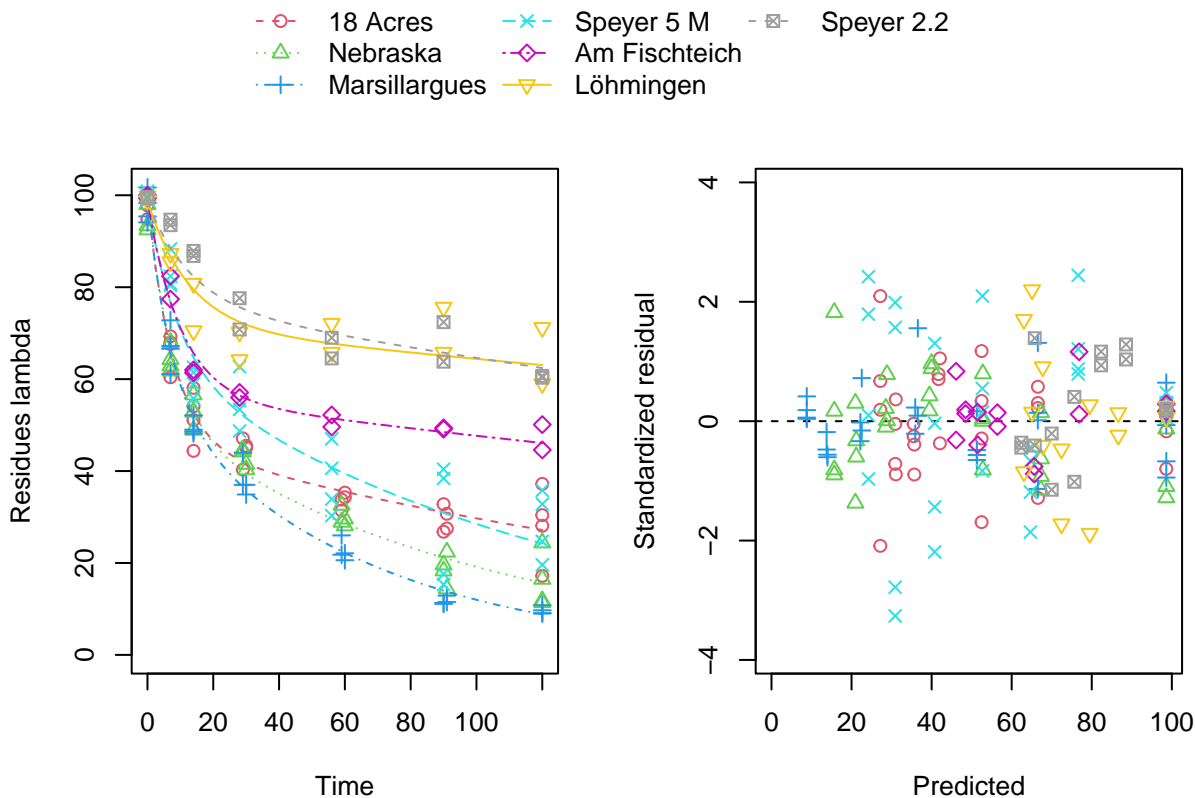


```
illparms(parent_best_pH_2)
parms(parent_best_pH_2, ci = TRUE) |> kable(digits = 3)
```

	estimate	lower	upper
lambda_free_0	98.616	96.664	100.568
log_k_lambda_free	-3.165	-3.574	-2.755
log_k_lambda_free_bound	-2.929	-3.208	-2.651
log_k_lambda_bound_free	-9.816	-14.184	-5.448
beta_pH(log_k_lambda_bound_free)	0.814	0.156	1.473
a.1	4.780	4.222	5.339
SD.log_k_lambda_free	0.512	0.238	0.786
SD.log_k_lambda_bound_free	0.585	0.190	0.981

Pathway fits

As an example of a pathway fit, a model with SFORB for the parent compound and parallel formation of two metabolites is set up.

```
if (!dir.exists("dlls")) dir.create("dlls")


m_sforb_sfo2 = mkinmod(
  lambda = mkinsub("SFORB", to = c("c_V", "c_XV")),
  c_V = mkinsub("SFO"),
  c_XV = mkinsub("SFO"),
  name = "sforb_sfo2",
  dll_dir = "dlls",
  overwrite = TRUE, quiet = TRUE
)
```
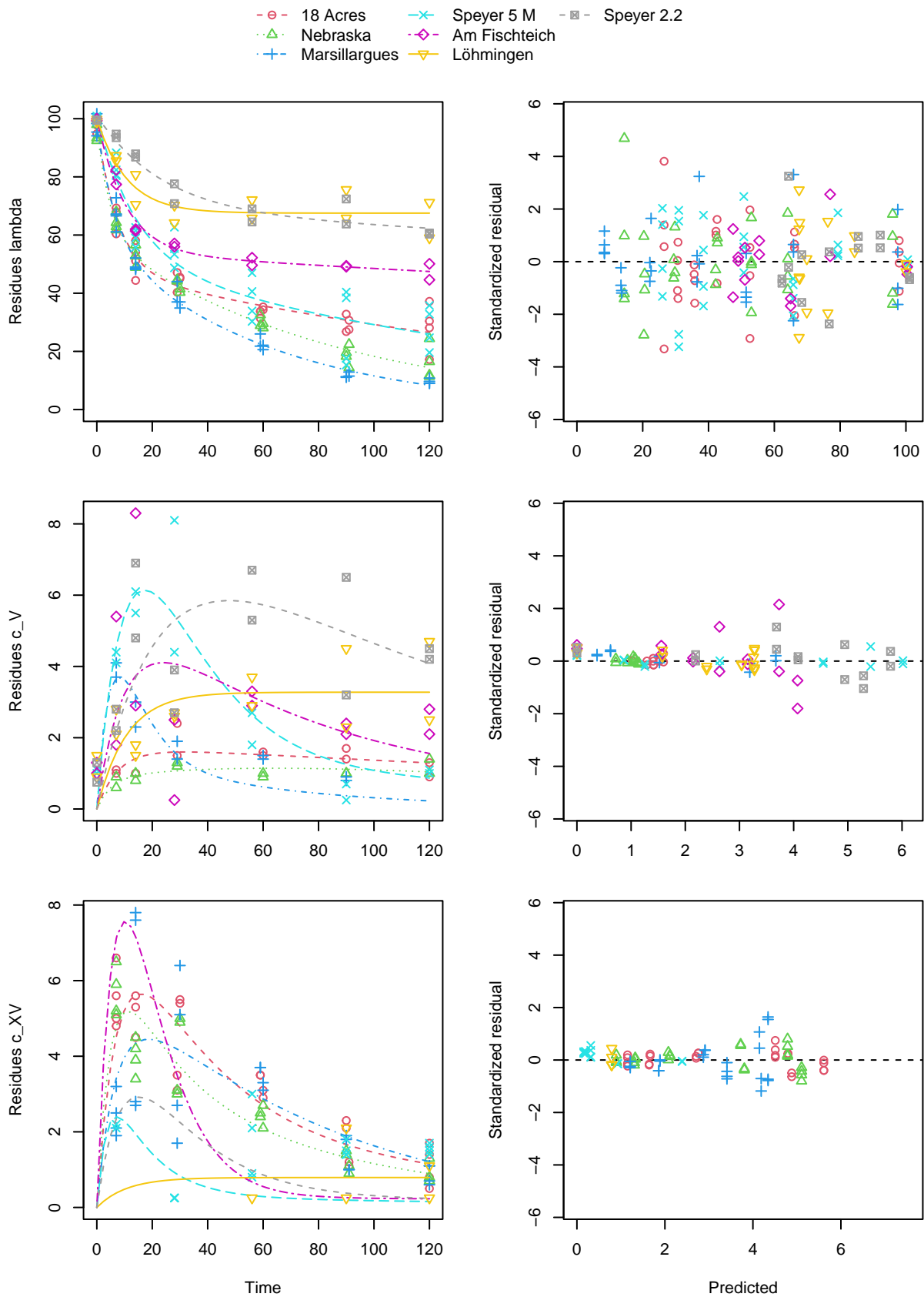
Separate evaluations of all datasets are performed with constant variance and using two-component error.

```
sforb_sep_const <- mmkin(list(sforb_path = m_sforb_sfo2), ds,
  cluster = cl, quiet = TRUE)
sforb_sep_tc <- update(sforb_sep_const, error_model = "tc")
```

The separate fits with constant variance are plotted.

```
plot(mixed(sforb_sep_const))
```

The two corresponding hierarchical fits, with the random effects for the parent degradation parameters excluded as discussed above, and including the covariate model that was identified for the parent degradation, are attempted below.

```
path_1 <- mhmkin(list(sforb_sep_const, sforb_sep_tc),
  no_random_effect = c("lambda_free_0", "log_k_lambda_free_bound"),
  covariates = covariates, covariate_models = list(log_k_lambda_bound_free ~ pH),
  cluster = cl)
```

```
status(path_1) |> kable()
```

	const	tc
sforb_path	OK	OK

The status information shows that both fits were successfully completed.

```
anova(path_1) |> kable(digits = 1)
```

	npar	AIC	BIC	Lik
sforb_path const	16	1876.2	1875.3	-922.1
sforb_path tc	17	1688.2	1687.3	-827.1

Model comparison shows that the two-component error model provides a much better fit.

```
illparms(path_1[["sforb_path", "tc"]])
```

```
[1] "sd(log_k_c_XV)"    "sd(f_lambda_ilr_2)"
```

Two ill-defined variance components are found. Therefore, the fit is repeated with the corresponding random effects removed.

```
path_1_refined <- update(path_1[["sforb_path", "tc"]],
  no_random_effect = c("lambda_free_0", "log_k_lambda_free_bound",
    "log_k_c_XV", "f_lambda_ilr_2"))
```

The empty output of the illparms function indicates that there are no ill-defined parameters remaining in the refined fit.

```
illparms(path_1_refined)
```

Below, the refined fit is plotted and the fitted parameters are shown together with their 95% confidence intervals.

```
plot(path_1_refined)
```

Legend:
- 18 Acres
- Nebraska
- Marsillargues
- Speyer 5 M
- Am Fischteich
- Löhmingen
- Speyer 2.2
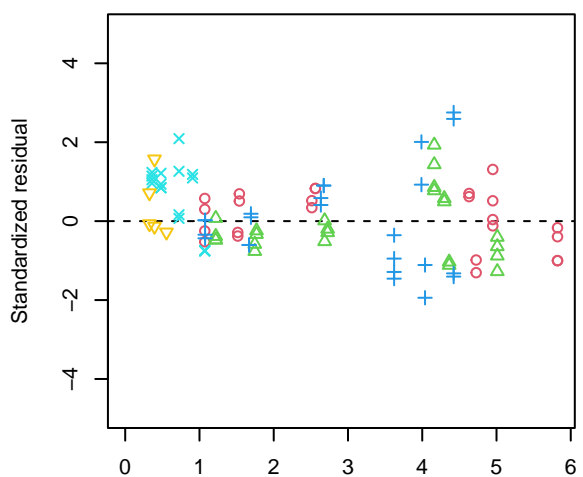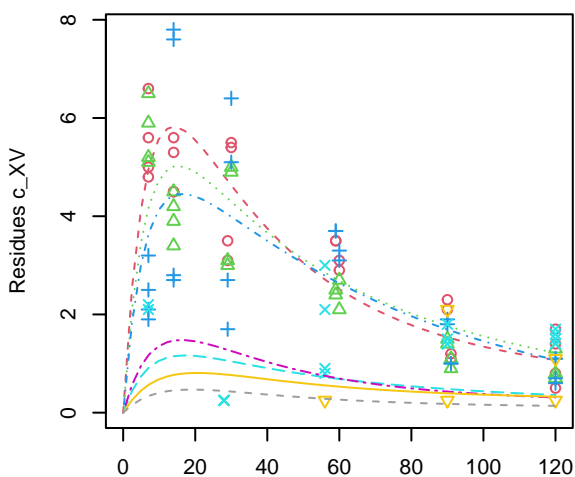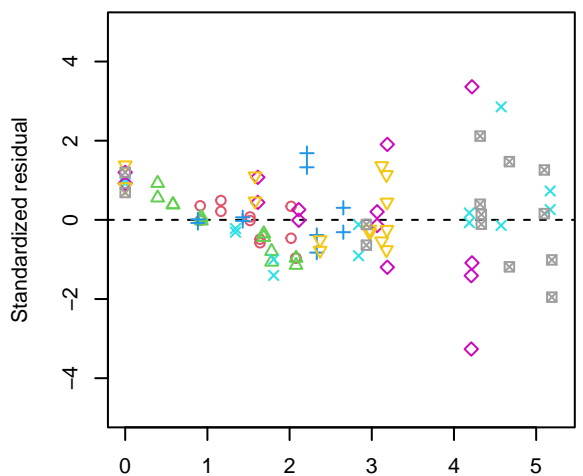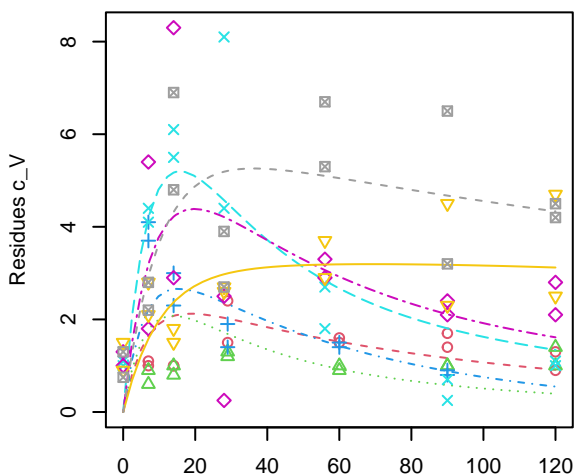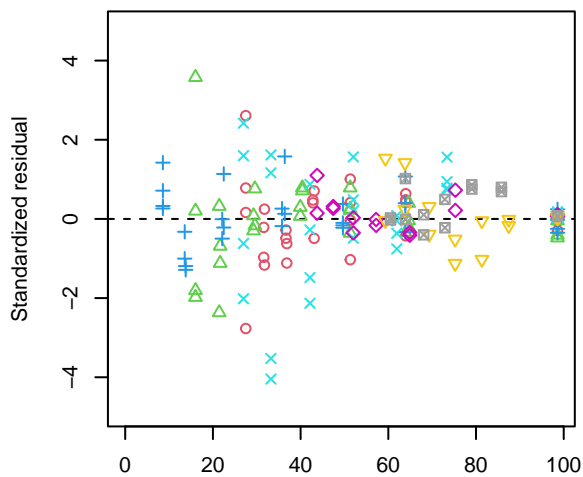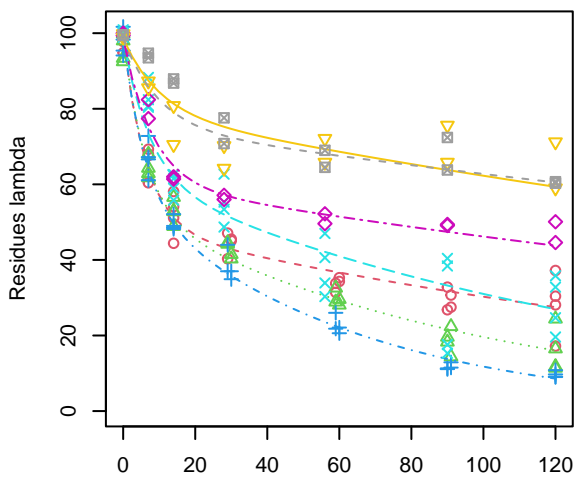
```
parms(path_1_refined, ci = TRUE) |> kable(digits = 3)
```

	estimate	lower	upper
lambda_free_0	98.589	93.645	103.534
log_k_lambda_free	-3.014	-3.474	-2.553
log_k_lambda_free_bound	-2.653	-2.961	-2.345
log_k_lambda_bound_free	-8.723	-11.291	-6.156
beta_pH(log_k_lambda_bound_free)	0.685	0.308	1.063
log_k_c_V	-3.980	-4.677	-3.283
log_k_c_XV	-3.504	-3.730	-3.279
f_lambda_ilr_1	0.317	-0.353	0.987
f_lambda_ilr_2	-1.770	-1.991	-1.548
a.1	1.084	0.953	1.216
b.1	0.129	0.113	0.146
SD.log_k_lambda_free	0.527	0.242	0.813
SD.log_k_lambda_bound_free	0.275	0.044	0.505
SD.log_k_c_V	0.778	0.273	1.283
SD.f_lambda_ilr_1	0.860	0.379	1.342

Appendix

Listings of initial parent fits

Listing 1: Hierarchical SFO fit with constant variance

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:           4.2.2
Date of fit:     Tue Jan  3 17:50:13 2023
Date of summary: Wed Jan  4 18:18:07 2023

Equations:
d_lambda/dt = - k_lambda * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 0.939 s
Using 300, 100 iterations and 8 chains

Variance model: Constant variance

Starting values for degradation parameters:
    lambda_0 log_k_lambda
      85.424       -4.655

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
             lambda_0 log_k_lambda
lambda_0        7.235        0.000
log_k_lambda    0.000        1.186

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  1178 1178 -584.2

Optimised parameters:
                   est.   lower  upper
lambda_0         85.327 81.5240 89.130
log_k_lambda     -4.662 -5.2667 -4.058
a.1               9.768  8.6243 10.911
SD.lambda_0       3.527 -0.3636  7.418
SD.log_k_lambda   0.797  0.3633  1.231

Correlation:
             lambd_0
log_k_lambda 0.0918

Random effects:
                  est.   lower upper
SD.lambda_0      3.527 -0.3636 7.418
SD.log_k_lambda  0.797  0.3633 1.231

Variance model:
     est. lower upper
a.1 9.768 8.624 10.91

Backtransformed parameters:
              est.    lower     upper
lambda_0 85.327208 81.52398 89.13044
k_lambda  0.009445  0.00516  0.01729

Estimated disappearance times:
        DT50  DT90
lambda 73.39 243.8
```

Listing 2: Hierarchical SFO fit with two-component error

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:         4.2.2
Date of fit:     Tue Jan  3 17:50:14 2023
Date of summary: Wed Jan  4 18:18:07 2023

Equations:
d_lambda/dt = - k_lambda * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 2.097 s
Using 300, 100 iterations and 8 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
    lambda_0 log_k_lambda
      81.903       -4.812

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
             lambda_0 log_k_lambda
lambda_0        9.812        0.000
log_k_lambda    0.000        1.108

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

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  1171 1170 -579.4

Optimised parameters:
                   est.    lower    upper
lambda_0        81.5922 77.64513 85.5393
log_k_lambda    -4.8364 -5.44951 -4.2234
a.1              5.7493  3.78825  7.7103
b.1              0.1370  0.09617  0.1778
SD.lambda_0      3.1857 -1.42084  7.7923
SD.log_k_lambda  0.8031  0.36291  1.2432

Correlation:
             lambd_0
log_k_lambda 0.1161

Random effects:
                  est.   lower upper
SD.lambda_0      3.1857 -1.4208 7.792
SD.log_k_lambda 0.8031  0.3629 1.243

Variance model:
     est.   lower  upper
a.1 5.749 3.78825 7.7103
b.1 0.137 0.09617 0.1778

Backtransformed parameters:
              est.     lower     upper
lambda_0 81.592195 77.645131 85.53926
k_lambda  0.007935  0.004298  0.01465

Estimated disappearance times:
        DT50  DT90
lambda 87.35 290.2
```

Listing 3: Hierarchical FOMC fit with constant variance

```
saemix version used for fitting:       3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:         4.2.2
Date of fit:     Tue Jan  3 17:50:13 2023
Date of summary: Wed Jan  4 18:18:07 2023

Equations:
d_lambda/dt = - (alpha/beta) * 1/((time/beta) + 1) * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 1.187 s
Using 300, 100 iterations and 8 chains

Variance model: Constant variance

Starting values for degradation parameters:
 lambda_0 log_alpha  log_beta
   98.750    -1.107     1.650

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
          lambda_0 log_alpha log_beta
lambda_0     3.026      0.00    0.000
log_alpha    0.000      1.21    0.000
log_beta     0.000      0.00    1.641

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  995.5 995.1 -490.7

Optimised parameters:
                est.    lower   upper
lambda_0     98.24884  96.2289 100.269
log_alpha    -1.06380  -1.5966  -0.531
log_beta      1.86676   1.1844   2.549
a.1           4.93686   4.3469   5.527
SD.lambda_0   0.06445 -56.8410  56.970
SD.log_alpha  0.69624   0.3127   1.080
SD.log_beta   0.79588   0.2783   1.313

Correlation:
          lambd_0 log_lph
log_alpha -0.0514
log_beta  -0.2212  0.1169

Random effects:
                est.    lower  upper
SD.lambda_0  0.06445 -56.8410 56.970
SD.log_alpha 0.69624   0.3127  1.080
SD.log_beta  0.79588   0.2783  1.313

Variance model:
     est. lower upper
a.1 4.937 4.347 5.527

Backtransformed parameters:
            est.   lower   upper
lambda_0 98.2488 96.2289 100.269
alpha     0.3451  0.2026   0.588
beta      6.4673  3.2687  12.796

Estimated disappearance times:
        DT50 DT90 DT50back
lambda 41.72 5100     1535
```

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:         4.2.2
Date of fit:     Tue Jan  3 17:50:15 2023
Date of summary: Wed Jan  4 18:18:07 2023

Equations:
d_lambda/dt = - (alpha/beta) * 1/((time/beta) + 1) * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 2.474 s
Using 300, 100 iterations and 8 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
 lambda_0 log_alpha  log_beta
   97.929    -1.054     1.734

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
          lambda_0 log_alpha log_beta
lambda_0     5.147     0.000    0.000
log_alpha    0.000     1.372    0.000
log_beta     0.000     0.000    1.927

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

Results:

Likelihood computed by importance sampling
    AIC BIC logLik
  997.5 997 -490.7

Optimised parameters:
                 est.      lower      upper
lambda_0      9.822e+01  96.19880 100.24953
log_alpha    -1.065e+00  -1.59819  -0.53164
log_beta      1.865e+00   1.18087   2.54836
a.1           4.950e+00   3.58401   6.31525
b.1           1.463e-05  -0.02303   0.02306
SD.lambda_0   4.766e-02 -81.97165  82.06697
SD.log_alpha  6.968e-01   0.31296   1.08065
SD.log_beta   7.976e-01   0.27901   1.31624

Correlation:
          lambd_0 log_lph
log_alpha -0.0513
log_beta  -0.2213  0.1169

Random effects:
                est.    lower  upper
SD.lambda_0  0.04766 -81.972 82.067
SD.log_alpha 0.69680   0.313  1.081
SD.log_beta  0.79763   0.279  1.316

Variance model:
          est.    lower    upper
a.1 4.950e+00  3.58401  6.31525
b.1 1.463e-05 -0.02303  0.02306

Backtransformed parameters:
            est.   lower     upper
lambda_0 98.2242 96.1988 100.2495
alpha     0.3448  0.2023    0.5876
beta      6.4534  3.2572   12.7861

Estimated disappearance times:
        DT50 DT90 DT50back
lambda 41.74 5127     1543
```

Listing 5: Hierarchical DFOP fit with constant variance

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:         4.2.2
Date of fit:     Tue Jan  3 17:50:14 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
           time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
           * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 1.815 s
Using 300, 100 iterations and 8 chains

Variance model: Constant variance

Starting values for degradation parameters:
lambda_0   log_k1   log_k2 g_qlogis
 99.0509  -2.2932  -5.5352  -0.3602

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
         lambda_0 log_k1 log_k2 g_qlogis
lambda_0    2.708 0.0000  0.000   0.0000
log_k1      0.000 0.7292  0.000   0.0000
log_k2      0.000 0.0000  1.821   0.0000
g_qlogis    0.000 0.0000  0.000   0.4459

Starting values for error model parameters:
a.1
  1


Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  986.4 985.9 -484.2

Optimised parameters:
                est.    lower      upper
lambda_0     98.81946  96.9255 100.71342
log_k1       -2.27102  -2.6755  -1.86653
log_k2       -5.81448  -6.9642  -4.66480
g_qlogis     -0.40756  -0.7606  -0.05453
a.1           4.62992   4.0654    5.19442
SD.lambda_0   0.04437 -73.0264  73.11518
SD.log_k1     0.45872   0.1509   0.76652
SD.log_k2     1.36571   0.5180   2.21338
SD.g_qlogis   0.39739   0.1269   0.66786


Correlation:
         lambd_0 log_k1  log_k2
log_k1    0.1672
log_k2    0.0296  0.1525
g_qlogis  0.0866 -0.2189 -0.1929

Random effects:
              est.    lower    upper
SD.lambda_0 0.04437 -73.0264 73.1152
SD.log_k1   0.45872   0.1509  0.7665
SD.log_k2   1.36571   0.5180  2.2134
SD.g_qlogis 0.39739   0.1269  0.6679

Variance model:
    est. lower upper
a.1 4.63 4.065 5.194

Backtransformed parameters:
             est.       lower      upper
lambda_0 98.819460 9.693e+01 1.007e+02
k1        0.103207 6.887e-02 1.547e-01
k2        0.002984 9.451e-04 9.421e-03
g         0.399497 3.185e-01 4.864e-01

Estimated disappearance times:
```

```
            DT50   DT90 DT50back DT50_k1 DT50_k2
lambda 61.83 600.7    180.8   6.716   232.3
```

Listing 6: Hierarchical DFOP fit with two-component error

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting: 1.2.2
R version used for fitting:      4.2.2
Date of fit:     Tue Jan  3 17:50:15 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
            time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
            * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 2.984 s
Using 300, 100 iterations and 8 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
lambda_0   log_k1    log_k2 g_qlogis
 99.1138  -2.2792   -5.5167  -0.3683

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
         lambda_0 log_k1 log_k2 g_qlogis
lambda_0    2.749 0.0000  0.000   0.0000
log_k1      0.000 0.7401  0.000   0.0000
log_k2      0.000 0.0000  1.798   0.0000
g_qlogis    0.000 0.0000  0.000   0.4461

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

Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  988.4 987.9 -484.2

Optimised parameters:
                 est.      lower      upper
lambda_0     9.861e+01  96.71049 100.50027
log_k1      -2.279e+00  -2.68597  -1.87255
log_k2      -5.819e+00  -6.95868  -4.68019
g_qlogis    -4.073e-01  -0.77904  -0.03555
a.1          4.635e+00   3.33113   5.93804
b.1          1.357e-05  -0.02177   0.02180
SD.lambda_0  6.608e-02 -52.08801  52.22017
SD.log_k1    4.599e-01   0.14936   0.77035
SD.log_k2    1.355e+00   0.51415   2.19626
SD.g_qlogis  4.244e-01   0.14166   0.70719

Correlation:
         lambd_0 log_k1  log_k2
log_k1    0.1685
log_k2    0.0304  0.1553
g_qlogis  0.0812 -0.2138 -0.1879

Random effects:
             est.    lower    upper
SD.lambda_0 0.06608 -52.0880 52.2202
SD.log_k1   0.45985   0.1494  0.7704
SD.log_k2   1.35520   0.5142  2.1963
SD.g_qlogis 0.42442   0.1417  0.7072

Variance model:
         est.    lower  upper
a.1 4.635e+00   3.33113 5.9380
b.1 1.357e-05 -0.02177 0.0218

Backtransformed parameters:
              est.     lower      upper
lambda_0 98.605381 9.671e+01 1.005e+02
k1        0.102360 6.816e-02 1.537e-01
k2        0.002969 9.504e-04 9.277e-03
g         0.399561 3.145e-01 4.911e-01
```

```
Estimated disappearance times:
        DT50  DT90 DT50back DT50_k1 DT50_k2
lambda 62.12 603.7    181.7   6.772   233.4
```

Listing 7: Hierarchical SFORB fit with constant variance

```
saemix version used for fitting:       3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:         4.2.2
Date of fit:     Tue Jan  3 17:50:14 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda_free/dt = - k_lambda_free * lambda_free - k_lambda_free_bound
           * lambda_free + k_lambda_bound_free * lambda_bound
d_lambda_bound/dt = + k_lambda_free_bound * lambda_free -
           k_lambda_bound_free * lambda_bound

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 1.797 s
Using 300, 100 iterations and 8 chains

Variance model: Constant variance

Starting values for degradation parameters:
         lambda_free_0      log_k_lambda_free log_k_lambda_free_bound
               99.051                 -3.135                  -2.983
log_k_lambda_bound_free
               -4.742

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                        lambda_free_0 log_k_lambda_free log_k_lambda_free_bound
lambda_free_0                   2.708            0.0000                  0.0000
log_k_lambda_free               0.000            0.8633                  0.0000
log_k_lambda_free_bound         0.000            0.0000                  0.6656
log_k_lambda_bound_free         0.000            0.0000                  0.0000
                        log_k_lambda_bound_free
lambda_free_0                             0.000
log_k_lambda_free                         0.000
log_k_lambda_free_bound                   0.000
log_k_lambda_bound_free                   1.736

Starting values for error model parameters:
a.1
  1


Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  986.8 986.3 -484.4

Optimised parameters:
                            est.    lower     upper
lambda_free_0            98.30172  96.3735 100.2300
log_k_lambda_free       -3.14361  -3.5532  -2.7340
log_k_lambda_free_bound -2.88903  -3.2083  -2.5698
log_k_lambda_bound_free -4.65588  -5.4839  -3.8279
a.1                      4.70334   4.1317   5.2749
SD.lambda_free_0         0.09938 -32.9988  33.1975
SD.log_k_lambda_free     0.50965   0.2292   0.7901
SD.log_k_lambda_free_bound 0.19967 -0.1792   0.5785
SD.log_k_lambda_bound_free 0.95337  0.3534   1.5534


Correlation:
                        lmbd__0 lg_k_l_ lg_k_lmbd_f_
log_k_lambda_free        0.2072
log_k_lambda_free_bound  0.1915  0.2925
log_k_lambda_bound_free -0.0031  0.0737   0.3223


Random effects:
                            est.    lower   upper
SD.lambda_free_0         0.09938 -32.9988 33.1975
SD.log_k_lambda_free     0.50965   0.2292  0.7901
SD.log_k_lambda_free_bound 0.19967  -0.1792  0.5785
SD.log_k_lambda_bound_free 0.95337   0.3534  1.5534


Variance model:
     est. lower upper
a.1 4.703 4.132 5.275
```

```
Backtransformed parameters:
                        est.      lower      upper
lambda_free_0       98.301718 96.373454 100.22998
k_lambda_free        0.043127  0.028632   0.06496
k_lambda_free_bound  0.055630  0.040426   0.07655
k_lambda_bound_free  0.009506  0.004153   0.02176


Estimated Eigenvalues of SFORB model(s):
lambda_b1 lambda_b2  lambda_g
 0.104333  0.003929  0.390399


Resulting formation fractions:
            ff
lambda_free  1


Estimated disappearance times:
        DT50  DT90 DT50back DT50_lambda_b1 DT50_lambda_b2
lambda 51.38 460.1    138.5          6.644          176.4
```

Listing 8: Hierarchical SFORB fit with two-component error

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:          4.2.2
Date of fit:     Tue Jan  3 17:50:16 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda_free/dt = - k_lambda_free * lambda_free - k_lambda_free_bound
          * lambda_free + k_lambda_bound_free * lambda_bound
d_lambda_bound/dt = + k_lambda_free_bound * lambda_free -
          k_lambda_bound_free * lambda_bound

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 3.125 s
Using 300, 100 iterations and 8 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
        lambda_free_0      log_k_lambda_free log_k_lambda_free_bound
              99.114                 -3.125                  -2.965
log_k_lambda_bound_free
              -4.718


Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                        lambda_free_0 log_k_lambda_free log_k_lambda_free_bound
lambda_free_0                   2.749            0.0000                  0.0000
log_k_lambda_free               0.000            0.8701                  0.0000
log_k_lambda_free_bound         0.000            0.0000                  0.6763
log_k_lambda_bound_free         0.000            0.0000                  0.0000
                        log_k_lambda_bound_free
lambda_free_0                             0.000
log_k_lambda_free                         0.000
log_k_lambda_free_bound                   0.000
log_k_lambda_bound_free                   1.718

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


Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  988.8 988.3 -484.4

Optimised parameters:
                              est.     lower      upper
lambda_free_0             9.825e+01  96.31126 100.18097
log_k_lambda_free       -3.166e+00  -3.57836  -2.75321
log_k_lambda_free_bound -2.921e+00  -3.21992  -2.62270
log_k_lambda_bound_free -4.669e+00  -5.51062  -3.82813
a.1                      4.724e+00   3.40854   6.04026
b.1                      1.399e-05  -0.02202   0.02205
SD.lambda_free_0         1.173e-01 -29.68086  29.91537
SD.log_k_lambda_free     5.152e-01   0.23486   0.79561
SD.log_k_lambda_free_bound 1.401e-01  -0.31367  0.59391
SD.log_k_lambda_bound_free 9.657e-01   0.36353  1.56792


Correlation:
                        lmbd__0 lg_k_l_ lg_k_lmbd_f_
log_k_lambda_free        0.2059
log_k_lambda_free_bound  0.2054  0.3014
log_k_lambda_bound_free -0.0027  0.0701   0.3420


Random effects:
                            est.    lower   upper
SD.lambda_free_0           0.1173 -29.6809 29.9154
SD.log_k_lambda_free       0.5152   0.2349  0.7956
SD.log_k_lambda_free_bound 0.1401  -0.3137  0.5939
SD.log_k_lambda_bound_free 0.9657   0.3635  1.5679


Variance model:
       est.    lower   upper
a.1 4.724e+00  3.40854 6.04026
```

```
b.1 1.399e-05 -0.02202 0.02205

Backtransformed parameters:
                       est.      lower      upper
lambda_free_0       98.246116 96.311263 100.18097
k_lambda_free        0.042181  0.027921   0.06372
k_lambda_free_bound  0.053863  0.039958   0.07261
k_lambda_bound_free  0.009378  0.004044   0.02175

Estimated Eigenvalues of SFORB model(s):
lambda_b1 lambda_b2  lambda_g
 0.101526  0.003896  0.392142

Resulting formation fractions:
            ff
lambda_free  1

Estimated disappearance times:
        DT50  DT90 DT50back DT50_lambda_b1 DT50_lambda_b2
lambda 51.24 463.2    139.4          6.827          177.9
```

Listings of refined parent fits

Listing 9: Refined hierarchical SFO fit with constant variance

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:        4.2.2
Date of fit:     Tue Jan  3 17:50:19 2023
Date of summary: Wed Jan  4 18:18:07 2023

Equations:
d_lambda/dt = - k_lambda * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 1.836 s
Using 300, 100 iterations and 8 chains

Variance model: Constant variance

Starting values for degradation parameters:
    lambda_0 log_k_lambda
      85.424      -4.655

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
           lambda_0 log_k_lambda
lambda_0         7.235        0.000
log_k_lambda     0.000        1.186

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  1177 1177 -584.7

Optimised parameters:
                est.    lower  upper
lambda_0        85.4275 82.6385 88.217
log_k_lambda    -4.6618 -5.2936 -4.030
a.1              9.9034  8.7714 11.035
SD.log_k_lambda 0.8337  0.3838  1.284

Correlation:
            lambd_0
log_k_lambda 0.1232

Random effects:
                 est.  lower upper
SD.log_k_lambda 0.8337 0.3838 1.284

Variance model:
     est. lower upper
a.1 9.903 8.771 11.04

Backtransformed parameters:
             est.      lower     upper
lambda_0 85.427522 82.638508 88.21654
k_lambda  0.009449  0.005024  0.01777

Estimated disappearance times:
        DT50  DT90
lambda 73.36 243.7
```

Listing 10: Refined hierarchical SFO fit with two-component error

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:          4.2.2
Date of fit:     Tue Jan  3 17:50:20 2023
Date of summary: Wed Jan  4 18:18:07 2023

Equations:
d_lambda/dt = - k_lambda * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 2.738 s
Using 300, 100 iterations and 8 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
    lambda_0 log_k_lambda
      81.903       -4.812

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
             lambda_0 log_k_lambda
lambda_0        9.812        0.000
log_k_lambda    0.000        1.108

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

Results:

Likelihood computed by importance sampling
   AIC  BIC logLik
  1170 1169 -579.8

Optimised parameters:
                  est.    lower   upper
lambda_0        81.6442 78.49543 84.7931
log_k_lambda    -4.8432 -5.48845 -4.1980
a.1              6.0238  4.03306  8.0144
b.1              0.1350  0.09463  0.1753
SD.log_k_lambda 0.8463  0.38624  1.3063

Correlation:
             lambd_0
log_k_lambda 0.1387

Random effects:
                 est.  lower upper
SD.log_k_lambda 0.8463 0.3862 1.306

Variance model:
     est.   lower  upper
a.1 6.024 4.03306 8.0144
b.1 0.135 0.09463 0.1753

Backtransformed parameters:
               est.     lower    upper
lambda_0 81.644245 78.495427 84.79306
k_lambda  0.007882  0.004134  0.01503

Estimated disappearance times:
        DT50  DT90
lambda 87.95 292.2
```

```
saemix version used for fitting:        3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:            4.2.2
Date of fit:      Tue Jan  3 17:50:19 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda/dt = - (alpha/beta) * 1/((time/beta) + 1) * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 2.034 s
Using 300, 100 iterations and 8 chains

Variance model: Constant variance

Starting values for degradation parameters:
 lambda_0 log_alpha  log_beta
   98.750    -1.107     1.650

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
          lambda_0 log_alpha log_beta
lambda_0     3.026      0.00    0.000
log_alpha    0.000      1.21    0.000
log_beta     0.000      0.00    1.641

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  993.6 993.3 -490.8

Optimised parameters:
                est.    lower     upper
lambda_0     98.4733 96.4528 100.4938
log_alpha    -1.0810 -1.6159  -0.5462
log_beta      1.8158  1.1409   2.4907
a.1           4.9326  4.3558   5.5095
SD.log_alpha 0.7000  0.3154   1.0847
SD.log_beta  0.7849  0.2723   1.2975


Correlation:
          lambd_0 log_lph
log_alpha -0.0481
log_beta  -0.2205  0.1149

Random effects:
               est.  lower upper
SD.log_alpha 0.7000 0.3154 1.085
SD.log_beta  0.7849 0.2723 1.297

Variance model:
     est. lower upper
a.1 4.933 4.356 5.509

Backtransformed parameters:
            est.   lower     upper
lambda_0 98.4733 96.4528 100.4938
alpha     0.3392  0.1987   0.5792
beta      6.1459  3.1295  12.0698

Estimated disappearance times:
        DT50 DT90 DT50back
lambda 41.27 5443     1638
```

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:         4.2.2
Date of fit:      Tue Jan  3 17:50:20 2023
Date of summary: Wed Jan  4 18:18:07 2023

Equations:
d_lambda/dt = - (alpha/beta) * 1/((time/beta) + 1) * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 3.184 s
Using 300, 100 iterations and 8 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
 lambda_0 log_alpha  log_beta
   97.929    -1.054     1.734

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
          lambda_0 log_alpha log_beta
lambda_0     5.147     0.000    0.000
log_alpha    0.000     1.372    0.000
log_beta     0.000     0.000    1.927

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

Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  995.6 995.2 -490.8

Optimised parameters:
                  est.     lower      upper
lambda_0       9.852e+01 96.50017 100.54304
log_alpha     -1.082e+00 -1.61128  -0.55249
log_beta       1.813e+00  1.14264   2.48344
a.1            4.935e+00  3.60622   6.26380
b.1            1.376e-05 -0.02163   0.02166
SD.log_alpha  6.925e-01  0.31167   1.07324
SD.log_beta   7.788e-01  0.26927   1.28825

Correlation:
          lambd_0 log_lph
log_alpha -0.0485
log_beta  -0.2216  0.1163

Random effects:
               est.  lower upper
SD.log_alpha 0.6925 0.3117 1.073
SD.log_beta  0.7788 0.2693 1.288

Variance model:
        est.     lower    upper
a.1 4.935e+00  3.60622 6.26380
b.1 1.376e-05 -0.02163 0.02166

Backtransformed parameters:
           est.   lower     upper
lambda_0 98.522 96.5002 100.5430
alpha     0.339  0.1996   0.5755
beta      6.129  3.1350  11.9824

Estimated disappearance times:
        DT50 DT90 DT50back
lambda 41.24 5459     1643
```

Listing 13: Refined hierarchical DFOP fit with constant variance

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:        4.2.2
Date of fit:     Tue Jan  3 17:50:19 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
            time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
            * lambda


Data:
154 observations of 1 variable(s) grouped in 7 datasets


Model predictions using solution type analytical


Fitted in 2.509 s
Using 300, 100 iterations and 8 chains


Variance model: Constant variance


Starting values for degradation parameters:
lambda_0   log_k1   log_k2 g_qlogis
 99.0509  -2.2932  -5.5352  -0.3602


Fixed degradation parameter values:
None


Starting values for random effects (square root of initial entries in omega):
         lambda_0 log_k1 log_k2 g_qlogis
lambda_0    2.708 0.0000  0.000   0.0000
log_k1      0.000 0.7292  0.000   0.0000
log_k2      0.000 0.0000  1.821   0.0000
g_qlogis    0.000 0.0000  0.000   0.4459


Starting values for error model parameters:
a.1
  1


Results:


Likelihood computed by importance sampling
    AIC   BIC logLik
  984.5 984.1 -484.2


Optimised parameters:
               est.    lower     upper
lambda_0    98.7702 96.8780 100.6623
log_k1      -2.2674 -2.6770  -1.8579
log_k2      -5.8055 -6.9372  -4.6737
g_qlogis    -0.4040 -0.7518  -0.0562
a.1          4.6272  4.0753   5.1791
SD.log_k1    0.4662  0.1556   0.7769
SD.log_k2    1.3464  0.5109   2.1820
SD.g_qlogis  0.3898  0.1224   0.6573


Correlation:
         lambd_0 log_k1  log_k2
log_k1    0.1648
log_k2    0.0306  0.1549
g_qlogis  0.0868 -0.2195 -0.2005


Random effects:
             est.  lower  upper
SD.log_k1   0.4662 0.1556 0.7769
SD.log_k2   1.3464 0.5109 2.1820
SD.g_qlogis 0.3898 0.1224 0.6573


Variance model:
     est. lower upper
a.1 4.627 4.075 5.179


Backtransformed parameters:
              est.     lower      upper
lambda_0 98.770170 96.878044 1.007e+02
k1        0.103577  0.068772 1.560e-01
k2        0.003011  0.000971 9.337e-03
g         0.400346  0.320420 4.860e-01


Estimated disappearance times:
        DT50   DT90 DT50back DT50_k1 DT50_k2
lambda 60.85  594.9    179.1   6.692   230.2
```
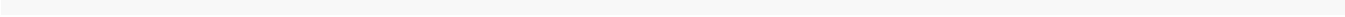
Listing 14: Refined hierarchical DFOP fit with two-component error

```
saemix version used for fitting:     3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:         4.2.2
Date of fit:     Tue Jan  3 17:50:21 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda/dt = - ((k1 * g * exp(-k1 * time) + k2 * (1 - g) * exp(-k2 *
          time)) / (g * exp(-k1 * time) + (1 - g) * exp(-k2 * time)))
          * lambda

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 4.107 s
Using 300, 100 iterations and 8 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
lambda_0   log_k1   log_k2 g_qlogis
 99.1138  -2.2792  -5.5167  -0.3683

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
        lambda_0 log_k1 log_k2 g_qlogis
lambda_0   2.749 0.0000  0.000   0.0000
log_k1     0.000 0.7401  0.000   0.0000
log_k2     0.000 0.0000  1.798   0.0000
g_qlogis   0.000 0.0000  0.000   0.4461

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

Results:

Likelihood computed by importance sampling
    AIC BIC logLik
  986.4 986 -484.2

Optimised parameters:
                est.     lower     upper
lambda_0     9.868e+01 96.79167 100.57409
log_k1      -2.270e+00 -2.68745  -1.85230
log_k2      -5.827e+00 -7.00299  -4.65123
g_qlogis    -4.083e-01 -0.74706  -0.06962
a.1          4.627e+00  3.36155   5.89203
b.1          1.251e-05 -0.02041   0.02044
SD.log_k1    4.801e-01  0.16485   0.79526
SD.log_k2    1.393e+00  0.52501   2.26017
SD.g_qlogis  3.770e-01  0.11491   0.63915

Correlation:
         lambd_0 log_k1  log_k2
log_k1    0.1615
log_k2    0.0299  0.1495
g_qlogis  0.0900 -0.2162 -0.2034

Random effects:
            est.  lower  upper
SD.log_k1   0.4801 0.1649 0.7953
SD.log_k2   1.3926 0.5250 2.2602
SD.g_qlogis 0.3770 0.1149 0.6391

Variance model:
        est.    lower    upper
a.1 4.627e+00  3.36155 5.89203
b.1 1.251e-05 -0.02041 0.02044

Backtransformed parameters:
            est.      lower      upper
lambda_0 98.682881 9.679e+01 100.57409
k1        0.103325 6.805e-02   0.15688
k2        0.002947 9.092e-04   0.00955
g         0.399311 3.215e-01   0.48260

Estimated disappearance times:
```

```
        DT50   DT90 DT50back DT50_k1 DT50_k2
lambda 62.68 608.5     183.2   6.708   235.2
```

Listing 15: Refined hierarchical SFORB fit with constant variance

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:         4.2.2
Date of fit:      Tue Jan  3 17:50:21 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda_free/dt = - k_lambda_free * lambda_free - k_lambda_free_bound
           * lambda_free + k_lambda_bound_free * lambda_bound
d_lambda_bound/dt = + k_lambda_free_bound * lambda_free -
           k_lambda_bound_free * lambda_bound

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 4.243 s
Using 300, 100 iterations and 8 chains

Variance model: Constant variance

Starting values for degradation parameters:
         lambda_free_0       log_k_lambda_free log_k_lambda_free_bound
              99.051                  -3.135                  -2.983
log_k_lambda_bound_free
              -4.742

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                     lambda_free_0 log_k_lambda_free log_k_lambda_free_bound
lambda_free_0                2.708            0.0000                  0.0000
log_k_lambda_free            0.000            0.8633                  0.0000
log_k_lambda_free_bound      0.000            0.0000                  0.6656
log_k_lambda_bound_free      0.000            0.0000                  0.0000
                     log_k_lambda_bound_free
lambda_free_0                          0.000
log_k_lambda_free                      0.000
log_k_lambda_free_bound                0.000
log_k_lambda_bound_free                1.736

Starting values for error model parameters:
a.1
  1

Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  982.7 982.3 -484.4

Optimised parameters:
                          est.    lower     upper
lambda_free_0           98.7892 96.8467 100.7317
log_k_lambda_free       -3.1243 -3.5332  -2.7155
log_k_lambda_free_bound -2.8459 -3.1220  -2.5698
log_k_lambda_bound_free -4.5942 -5.4165  -3.7719
a.1                      4.7392  4.1847   5.2937
SD.log_k_lambda_free     0.5095  0.2363   0.7826
SD.log_k_lambda_bound_free  0.9575  0.3824   1.5327

Correlation:
                        lmbd__0 lg_k_l_ lg_k_lmbd_f_
log_k_lambda_free        0.2050
log_k_lambda_free_bound  0.2053  0.3259
log_k_lambda_bound_free -0.0107  0.0657  0.3485

Random effects:
                          est.  lower  upper
SD.log_k_lambda_free    0.5095 0.2363 0.7826
SD.log_k_lambda_bound_free 0.9575 0.3824 1.5327

Variance model:
     est. lower upper
a.1 4.739 4.185 5.294

Backtransformed parameters:
                      est.      lower      upper
lambda_free_0     98.78919  96.846671 100.73170
k_lambda_free      0.04397   0.029212   0.06617
```

```
k_lambda_free_bound  0.05808  0.044071   0.07655
k_lambda_bound_free  0.01011  0.004443   0.02301


Estimated Eigenvalues of SFORB model(s):
lambda_b1 lambda_b2  lambda_g
 0.108047  0.004114  0.383446

Resulting formation fractions:
            ff
lambda_free  1

Estimated disappearance times:
        DT50   DT90 DT50back DT50_lambda_b1 DT50_lambda_b2
lambda 51.64 442.1    133.1          6.415          168.5
```

Listing 16: Refined hierarchical SFORB fit with two-component error

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:        4.2.2
Date of fit:     Tue Jan  3 17:50:23 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda_free/dt = - k_lambda_free * lambda_free - k_lambda_free_bound
           * lambda_free + k_lambda_bound_free * lambda_bound
d_lambda_bound/dt = + k_lambda_free_bound * lambda_free -
           k_lambda_bound_free * lambda_bound

Data:
154 observations of 1 variable(s) grouped in 7 datasets

Model predictions using solution type analytical

Fitted in 5.798 s
Using 300, 100 iterations and 8 chains


Variance model: Two-component variance function

Starting values for degradation parameters:
        lambda_free_0      log_k_lambda_free log_k_lambda_free_bound
             99.114                 -3.125                 -2.965
log_k_lambda_bound_free
             -4.718


Fixed degradation parameter values:
None


Starting values for random effects (square root of initial entries in omega):
                       lambda_free_0 log_k_lambda_free log_k_lambda_free_bound
lambda_free_0                  2.749            0.0000                  0.0000
log_k_lambda_free              0.000            0.8701                  0.0000
log_k_lambda_free_bound        0.000            0.0000                  0.6763
log_k_lambda_bound_free        0.000            0.0000                  0.0000
                       log_k_lambda_bound_free
lambda_free_0                            0.000
log_k_lambda_free                        0.000
log_k_lambda_free_bound                  0.000
log_k_lambda_bound_free                  1.718


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


Results:

Likelihood computed by importance sampling
    AIC   BIC logLik
  984.7 984.3 -484.4

Optimised parameters:
                             est.     lower      upper
lambda_free_0             9.874e+01 96.79810 100.67433
log_k_lambda_free        -3.143e+00 -3.55035  -2.73632
log_k_lambda_free_bound  -2.892e+00 -3.16506  -2.61989
log_k_lambda_bound_free  -4.653e+00 -5.49433  -3.81203
a.1                       4.733e+00  3.45422   6.01261
b.1                       1.139e-05 -0.02069   0.02071
SD.log_k_lambda_free      5.085e-01  0.23602   0.78090
SD.log_k_lambda_bound_free 9.722e-01 0.38433   1.55999


Correlation:
                       lmbd__0 lg_k_l_ lg_k_lmbd_f_
log_k_lambda_free       0.2048
log_k_lambda_free_bound 0.2123  0.3206
log_k_lambda_bound_free -0.0062 0.0661  0.3550


Random effects:
                             est.  lower  upper
SD.log_k_lambda_free       0.5085 0.2360 0.7809
SD.log_k_lambda_bound_free 0.9722 0.3843 1.5600


Variance model:
      est.     lower   upper
a.1 4.733e+00  3.45422 6.01261
b.1 1.139e-05 -0.02069 0.02071


Backtransformed parameters:
                          est.    lower     upper
```

```
lambda_free_0        98.736214 96.79810 100.67433
k_lambda_free         0.043139  0.02871   0.06481
k_lambda_free_bound   0.055439  0.04221   0.07281
k_lambda_bound_free   0.009531  0.00411   0.02210


Estimated Eigenvalues of SFORB model(s):
lambda_b1 lambda_b2  lambda_g
 0.104161  0.003947  0.391077


Resulting formation fractions:
            ff
lambda_free  1


Estimated disappearance times:
        DT50  DT90 DT50back DT50_lambda_b1 DT50_lambda_b2
lambda 50.92 457.6    137.8          6.655          175.6
```

Listings of pathway fits

Listing 17: Hierarchical fit of SFORB-SFO2 with constant variance

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:      4.2.2
Date of fit:    Wed Jan  4 17:55:21 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda_free/dt = - k_lambda_free * lambda_free - k_lambda_free_bound
          * lambda_free + k_lambda_bound_free * lambda_bound
d_lambda_bound/dt = + k_lambda_free_bound * lambda_free -
          k_lambda_bound_free * lambda_bound
d_c_V/dt = + f_lambda_free_to_c_V * k_lambda_free * lambda_free - k_c_V
          * c_V
d_c_XV/dt = + f_lambda_free_to_c_XV * k_lambda_free * lambda_free -
          k_c_XV * c_XV

Data:
339 observations of 3 variable(s) grouped in 7 datasets

Model predictions using solution type deSolve

Fitted in 1135.43 s
Using 300, 100 iterations and 8 chains

Variance model: Constant variance

Starting values for degradation parameters:
        lambda_free_0      log_k_lambda_free log_k_lambda_free_bound
              99.0737              -3.1284                -2.9708
log_k_lambda_bound_free            log_k_c_V              log_k_c_XV
              -4.6945              -3.9804                -3.3850
        f_lambda_ilr_1      f_lambda_ilr_2
              -0.3475              -1.2585

Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                        lambda_free_0 log_k_lambda_free log_k_lambda_free_bound
lambda_free_0                   2.727            0.0000                  0.0000
log_k_lambda_free               0.000            0.8613                  0.0000
log_k_lambda_free_bound         0.000            0.0000                  0.6612
log_k_lambda_bound_free         0.000            0.0000                  0.0000
log_k_c_V                       0.000            0.0000                  0.0000
log_k_c_XV                      0.000            0.0000                  0.0000
f_lambda_ilr_1                  0.000            0.0000                  0.0000
f_lambda_ilr_2                  0.000            0.0000                  0.0000
                        log_k_lambda_bound_free log_k_c_V log_k_c_XV
lambda_free_0                             0.000     0.000     0.0000
log_k_lambda_free                        0.000     0.000     0.0000
log_k_lambda_free_bound                  0.000     0.000     0.0000
log_k_lambda_bound_free                  1.655     0.000     0.0000
log_k_c_V                                0.000     1.734     0.0000
log_k_c_XV                               0.000     0.000     0.4138
f_lambda_ilr_1                           0.000     0.000     0.0000
f_lambda_ilr_2                           0.000     0.000     0.0000
                        f_lambda_ilr_1 f_lambda_ilr_2
lambda_free_0                    0.000          0.000
log_k_lambda_free                0.000          0.000
log_k_lambda_free_bound          0.000          0.000
log_k_lambda_bound_free          0.000          0.000
log_k_c_V                        0.000          0.000
log_k_c_XV                       0.000          0.000
f_lambda_ilr_1                   1.232          0.000
f_lambda_ilr_2                   0.000          1.239

Starting values for error model parameters:
a.1
  1


Results:


Likelihood computed by importance sampling
   AIC  BIC logLik
  1876 1875 -922.1


Optimised parameters:
                              est.      lower    upper
lambda_free_0             98.887148  97.52765 100.2467
log_k_lambda_free         -3.122365  -3.50942  -2.7353
```

```
log_k_lambda_free_bound          -2.859822  -3.05135  -2.6683
log_k_lambda_bound_free          -9.391974 -14.56506  -4.2189
beta_pH(log_k_lambda_bound_free)  0.746946  -0.05139   1.5453
log_k_c_V                        -3.167309  -4.72612  -1.6085
log_k_c_XV                       -3.370081  -3.97904  -2.7611
f_lambda_ilr_1                    0.153288  -0.29613   0.6027
f_lambda_ilr_2                   -1.323117  -1.69285  -0.9534
a.1                               3.314571   3.05479   3.5744
SD.log_k_lambda_free              0.501480   0.23569   0.7673
SD.log_k_lambda_bound_free        0.785855   0.32271   1.2490
SD.log_k_c_V                      1.629993   0.56680   2.6932
SD.log_k_c_XV                     0.009687 -12.72984  12.7492
SD.f_lambda_ilr_1                 0.030929  -3.94350   4.0054
SD.f_lambda_ilr_2                 0.005680 -14.69266  14.7040

Correlation:
                                 lmbd__0 lg_k_l_ lg_k_lmbd_f_ lg_k_lmbd_b_
log_k_lambda_free                 0.1503
log_k_lambda_free_bound           0.2054  0.2370
log_k_lambda_bound_free          -0.0018  0.0137  0.1313
beta_pH(log_k_lambda_bound_free)  0.0007 -0.0083 -0.0916      -0.9918
log_k_c_V                        -0.0283 -0.0124 -0.0206       0.0082
log_k_c_XV                       -0.0412 -0.0119 -0.0161      -0.0020
f_lambda_ilr_1                   -0.0327 -0.0129 -0.0209       0.0095
f_lambda_ilr_2                   -0.1511 -0.0377 -0.0493       0.0088
                                 b_H(___ lg_k__V lg___XV f_lm__1
log_k_lambda_free
log_k_lambda_free_bound
log_k_lambda_bound_free
beta_pH(log_k_lambda_bound_free)
log_k_c_V                        -0.0068
log_k_c_XV                        0.0027  0.0018
f_lambda_ilr_1                   -0.0083  0.3911 -0.4899
f_lambda_ilr_2                   -0.0065  0.3994  0.4757  0.2553

Random effects:
                           est.    lower   upper
SD.log_k_lambda_free       0.501480  0.2357  0.7673
SD.log_k_lambda_bound_free 0.785855  0.3227  1.2490
SD.log_k_c_V               1.629993  0.5668  2.6932
SD.log_k_c_XV              0.009687 -12.7298 12.7492
SD.f_lambda_ilr_1          0.030929  -3.9435  4.0054
SD.f_lambda_ilr_2          0.005680 -14.6927 14.7040

Variance model:
     est. lower upper
a.1 3.315 3.055 3.574

Backtransformed parameters:
                         est.      lower      upper
lambda_free_0          9.889e+01 9.753e+01 100.24665
k_lambda_free          4.405e-02 2.991e-02   0.06487
k_lambda_free_bound    5.728e-02 4.730e-02   0.06937
k_lambda_bound_free    8.339e-05 4.726e-07   0.01471
k_c_V                  4.212e-02 8.861e-03   0.20019
k_c_XV                 3.439e-02 1.870e-02   0.06322
f_lambda_free_to_c_V   1.577e-01 8.363e-02   0.20615
f_lambda_free_to_c_XV  1.270e-01 8.363e-02   0.20615

Estimated Eigenvalues of SFORB model(s):
lambda_b1 lambda_b2  lambda_g
1.014e-01 3.624e-05 4.343e-01

Resulting formation fractions:
                   ff
lambda_free_c_V  0.1577
lambda_free_c_XV 0.1270
lambda_free_sink 0.7153
lambda_free      1.0000

Estimated disappearance times:
        DT50      DT90 DT50back DT50_lambda_b1 DT50_lambda_b2
lambda 3405.29 47819.64    14395          6.837          19129
c_V      16.46    54.67       NA             NA             NA
c_XV     20.16    66.96       NA             NA             NA
```

Listing 18: Hierarchical fit of SFORB-SFO2 with two-component error

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:        4.2.2
Date of fit:     Wed Jan  4 17:55:38 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda_free/dt = - k_lambda_free * lambda_free - k_lambda_free_bound
          * lambda_free + k_lambda_bound_free * lambda_bound
d_lambda_bound/dt = + k_lambda_free_bound * lambda_free -
          k_lambda_bound_free * lambda_bound
d_c_V/dt = + f_lambda_free_to_c_V * k_lambda_free * lambda_free - k_c_V
          * c_V
d_c_XV/dt = + f_lambda_free_to_c_XV * k_lambda_free * lambda_free -
          k_c_XV * c_XV

Data:
339 observations of 3 variable(s) grouped in 7 datasets

Model predictions using solution type deSolve

Fitted in 1152.995 s
Using 300, 100 iterations and 8 chains


Variance model: Two-component variance function

Starting values for degradation parameters:
         lambda_free_0     log_k_lambda_free log_k_lambda_free_bound
              98.7580               -3.0608                 -2.8878
log_k_lambda_bound_free              log_k_c_V             log_k_c_XV
              -4.6321               -4.0472                 -2.9080
        f_lambda_ilr_1       f_lambda_ilr_2
              -0.3637               -1.2041


Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                        lambda_free_0 log_k_lambda_free log_k_lambda_free_bound
lambda_free_0                    3.85            0.0000                  0.0000
log_k_lambda_free                0.00            0.9467                  0.0000
log_k_lambda_free_bound          0.00            0.0000                  0.7163
log_k_lambda_bound_free          0.00            0.0000                  0.0000
log_k_c_V                        0.00            0.0000                  0.0000
log_k_c_XV                       0.00            0.0000                  0.0000
f_lambda_ilr_1                   0.00            0.0000                  0.0000
f_lambda_ilr_2                   0.00            0.0000                  0.0000
                        log_k_lambda_bound_free log_k_c_V log_k_c_XV
lambda_free_0                             0.000     0.000      0.000
log_k_lambda_free                         0.000     0.000      0.000
log_k_lambda_free_bound                   0.000     0.000      0.000
log_k_lambda_bound_free                   1.396     0.000      0.000
log_k_c_V                                 0.000     1.917      0.000
log_k_c_XV                                0.000     0.000      1.633
f_lambda_ilr_1                            0.000     0.000      0.000
f_lambda_ilr_2                            0.000     0.000      0.000
                        f_lambda_ilr_1 f_lambda_ilr_2
lambda_free_0                    0.000          0.000
log_k_lambda_free                0.000          0.000
log_k_lambda_free_bound          0.000          0.000
log_k_lambda_bound_free          0.000          0.000
log_k_c_V                        0.000          0.000
log_k_c_XV                       0.000          0.000
f_lambda_ilr_1                   1.224          0.000
f_lambda_ilr_2                   0.000          1.442


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


Results:


Likelihood computed by importance sampling
   AIC  BIC logLik
  1688 1687 -827.1


Optimised parameters:
                                est.      lower     upper
lambda_free_0                 98.5616   93.48658 103.6366
log_k_lambda_free             -3.0087   -3.47861  -2.5389
log_k_lambda_free_bound       -2.6314   -2.93927  -2.3236
log_k_lambda_bound_free       -8.5928  -10.94129  -6.2443
```

```
beta_pH(log_k_lambda_bound_free)  0.6704   0.32741   1.0133
log_k_c_V                                  -4.0864  -4.82578  -3.3471
log_k_c_XV                                 -3.5968  -3.93235  -3.2613
f_lambda_ilr_1                              0.2374  -0.48682   0.9617
f_lambda_ilr_2                             -1.7557  -2.03613  -1.4753
a.1                                         1.0031   0.87687   1.1293
b.1                                         0.1335   0.11695   0.1501
SD.log_k_lambda_free                        0.5407   0.24800   0.8333
SD.log_k_lambda_bound_free                  0.2289   0.01482   0.4430
SD.log_k_c_V                                0.8384   0.28011   1.3967
SD.log_k_c_XV                               0.2409  -0.04406   0.5259
SD.f_lambda_ilr_1                           0.9146   0.38540   1.4437
SD.f_lambda_ilr_2                           0.1854  -0.02819   0.3990


Correlation:
                                 lmbd__0 lg_k_l_ lg_k_lmbd_f_ lg_k_lmbd_b_
log_k_lambda_free                 0.3331
log_k_lambda_free_bound           0.1416  0.3945
log_k_lambda_bound_free          -0.0239  0.0140  0.2445
beta_pH(log_k_lambda_bound_free) -0.0031 -0.0112 -0.1874      -0.9918
log_k_c_V                        -0.1626 -0.1090 -0.0769       0.1008
log_k_c_XV                       -0.2258 -0.1284 -0.1040       0.0339
f_lambda_ilr_1                   -0.0619 -0.0382 -0.0137       0.0436
f_lambda_ilr_2                   -0.5408 -0.2445 -0.1504       0.0374
                                 b_H(___ lg_k__V lg___XV f_lm__1
log_k_lambda_free
log_k_lambda_free_bound
log_k_lambda_bound_free
beta_pH(log_k_lambda_bound_free)
log_k_c_V                        -0.0875
log_k_c_XV                       -0.0214  0.0707
f_lambda_ilr_1                   -0.0400  0.0765 -0.0714
f_lambda_ilr_2                   -0.0149  0.2554  0.3244 -0.0657


Random effects:
                            est.    lower  upper
SD.log_k_lambda_free       0.5407  0.24800 0.8333
SD.log_k_lambda_bound_free 0.2289  0.01482 0.4430
SD.log_k_c_V               0.8384  0.28011 1.3967
SD.log_k_c_XV              0.2409 -0.04406 0.5259
SD.f_lambda_ilr_1          0.9146  0.38540 1.4437
SD.f_lambda_ilr_2          0.1854 -0.02819 0.3990


Variance model:
     est.  lower  upper
a.1 1.0031 0.8769 1.1293
b.1 0.1335 0.1169 0.1501


Backtransformed parameters:
                         est.     lower     upper
lambda_free_0         9.856e+01 9.349e+01 1.036e+02
k_lambda_free         4.935e-02 3.085e-02 7.896e-02
k_lambda_free_bound   7.198e-02 5.290e-02 9.792e-02
k_lambda_bound_free   1.854e-04 1.771e-05 1.941e-03
k_c_V                 1.680e-02 8.020e-03 3.519e-02
k_c_XV                2.741e-02 1.960e-02 3.834e-02
f_lambda_free_to_c_V  1.114e-01 5.318e-02 1.104e-01
f_lambda_free_to_c_XV 7.964e-02 5.318e-02 1.104e-01


Estimated Eigenvalues of SFORB model(s):
lambda_b1 lambda_b2  lambda_g
1.214e-01 7.536e-05 4.060e-01


Resulting formation fractions:
                   ff
lambda_free_c_V  0.11142
lambda_free_c_XV 0.07964
lambda_free_sink 0.80893
lambda_free      1.00000


Estimated disappearance times:
           DT50    DT90 DT50back DT50_lambda_b1 DT50_lambda_b2
lambda 2284.97 23641.2     7117          5.708           9197
c_V      41.26   137.1       NA             NA             NA
c_XV     25.29    84.0       NA             NA             NA
```

Listing 19: Refined hierarchical fit of SFORB-SFO2 with two-component error

```
saemix version used for fitting:      3.2
mkin version used for pre-fitting:  1.2.2
R version used for fitting:          4.2.2
Date of fit:      Wed Jan  4 18:18:06 2023
Date of summary: Wed Jan  4 18:18:07 2023


Equations:
d_lambda_free/dt = - k_lambda_free * lambda_free - k_lambda_free_bound
          * lambda_free + k_lambda_bound_free * lambda_bound
d_lambda_bound/dt = + k_lambda_free_bound * lambda_free -
          k_lambda_bound_free * lambda_bound
d_c_V/dt = + f_lambda_free_to_c_V * k_lambda_free * lambda_free - k_c_V
          * c_V
d_c_XV/dt = + f_lambda_free_to_c_XV * k_lambda_free * lambda_free -
          k_c_XV * c_XV

Data:
339 observations of 3 variable(s) grouped in 7 datasets

Model predictions using solution type deSolve

Fitted in 1347.491 s
Using 300, 100 iterations and 8 chains

Variance model: Two-component variance function

Starting values for degradation parameters:
          lambda_free_0      log_k_lambda_free log_k_lambda_free_bound
              98.7580                -3.0608                 -2.8878
log_k_lambda_bound_free              log_k_c_V               log_k_c_XV
              -4.6321                -4.0472                 -2.9080
        f_lambda_ilr_1     f_lambda_ilr_2
              -0.3637                -1.2041


Fixed degradation parameter values:
None

Starting values for random effects (square root of initial entries in omega):
                     lambda_free_0 log_k_lambda_free log_k_lambda_free_bound
lambda_free_0                 3.85            0.0000                  0.0000
log_k_lambda_free             0.00            0.9467                  0.0000
log_k_lambda_free_bound       0.00            0.0000                  0.7163
log_k_lambda_bound_free       0.00            0.0000                  0.0000
log_k_c_V                     0.00            0.0000                  0.0000
log_k_c_XV                    0.00            0.0000                  0.0000
f_lambda_ilr_1                0.00            0.0000                  0.0000
f_lambda_ilr_2                0.00            0.0000                  0.0000
                     log_k_lambda_bound_free log_k_c_V log_k_c_XV
lambda_free_0                          0.000     0.000      0.000
log_k_lambda_free                      0.000     0.000      0.000
log_k_lambda_free_bound                0.000     0.000      0.000
log_k_lambda_bound_free                1.396     0.000      0.000
log_k_c_V                              0.000     1.917      0.000
log_k_c_XV                             0.000     0.000      1.633
f_lambda_ilr_1                         0.000     0.000      0.000
f_lambda_ilr_2                         0.000     0.000      0.000
                     f_lambda_ilr_1 f_lambda_ilr_2
lambda_free_0                 0.000          0.000
log_k_lambda_free             0.000          0.000
log_k_lambda_free_bound       0.000          0.000
log_k_lambda_bound_free       0.000          0.000
log_k_c_V                     0.000          0.000
log_k_c_XV                    0.000          0.000
f_lambda_ilr_1                1.224          0.000
f_lambda_ilr_2                0.000          1.442

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


Results:


Likelihood computed by importance sampling
   AIC  BIC logLik
  1690 1689 -829.8

Optimised parameters:
                                 est.      lower     upper
lambda_free_0                 98.5893   93.64479 103.5339
log_k_lambda_free             -3.0137   -3.47422  -2.5532
log_k_lambda_free_bound       -2.6526   -2.96065  -2.3446
log_k_lambda_bound_free       -8.7235  -11.29055  -6.1564
```

```
beta_pH(log_k_lambda_bound_free)  0.6851  0.30761   1.0626
log_k_c_V                                 -3.9804 -4.67738  -3.2834
log_k_c_XV                                -3.5044 -3.73014  -3.2786
f_lambda_ilr_1                             0.3173 -0.35257   0.9872
f_lambda_ilr_2                            -1.7699 -1.99140  -1.5484
a.1                                        1.0844  0.95310   1.2158
b.1                                        0.1293  0.11316   0.1455
SD.log_k_lambda_free                       0.5275  0.24164   0.8133
SD.log_k_lambda_bound_free                 0.2747  0.04441   0.5051
SD.log_k_c_V                               0.7777  0.27275   1.2826
SD.f_lambda_ilr_1                          0.8601  0.37862   1.3416

Correlation:
                                  lmbd__0 lg_k_l_ lg_k_lmbd_f_ lg_k_lmbd_b_
log_k_lambda_free                  0.3374
log_k_lambda_free_bound            0.1545  0.4041
log_k_lambda_bound_free           -0.0230  0.0139   0.2317
beta_pH(log_k_lambda_bound_free)  -0.0005 -0.0103  -0.1767      -0.9917
log_k_c_V                         -0.1654 -0.1136  -0.0833       0.0998
log_k_c_XV                        -0.3415 -0.1985  -0.1730       0.0464
f_lambda_ilr_1                    -0.0785 -0.0477  -0.0181       0.0439
f_lambda_ilr_2                    -0.6443 -0.2944  -0.1921       0.0529
                                  b_H(___ lg_k__V lg___XV f_lm__1
log_k_lambda_free
log_k_lambda_free_bound
log_k_lambda_bound_free
beta_pH(log_k_lambda_bound_free)
log_k_c_V                         -0.0866
log_k_c_XV                        -0.0318  0.1003
f_lambda_ilr_1                    -0.0392  0.0856 -0.0853
f_lambda_ilr_2                    -0.0296  0.3351  0.5358  0.0109

Random effects:
                            est.   lower  upper
SD.log_k_lambda_free       0.5275 0.24164 0.8133
SD.log_k_lambda_bound_free 0.2747 0.04441 0.5051
SD.log_k_c_V               0.7777 0.27275 1.2826
SD.f_lambda_ilr_1          0.8601 0.37862 1.3416

Variance model:
      est.  lower  upper
a.1 1.0844 0.9531 1.2158
b.1 0.1293 0.1132 0.1455

Backtransformed parameters:
                          est.      lower     upper
lambda_free_0          9.859e+01 9.364e+01 103.53388
k_lambda_free          4.911e-02 3.099e-02   0.07783
k_lambda_free_bound    7.047e-02 5.179e-02   0.09589
k_lambda_bound_free    1.627e-04 1.249e-05   0.00212
k_c_V                  1.868e-02 9.303e-03   0.03750
k_c_XV                 3.007e-02 2.399e-02   0.03768
f_lambda_free_to_c_V   1.160e-01 5.645e-02   0.10067
f_lambda_free_to_c_XV  7.406e-02 5.645e-02   0.10067

Estimated Eigenvalues of SFORB model(s):
lambda_b1 lambda_b2  lambda_g
1.197e-01 6.678e-05 4.100e-01

Resulting formation fractions:
                     ff
lambda_free_c_V  0.11600
lambda_free_c_XV 0.07406
lambda_free_sink 0.80993
lambda_free      1.00000

Estimated disappearance times:
          DT50     DT90 DT50back DT50_lambda_b1 DT50_lambda_b2
lambda 2477.68 26580.49     8002          5.792          10380
c_V      37.11   123.28       NA             NA             NA
c_XV     23.05    76.58       NA             NA             NA
```

Session info

```
R version 4.2.2 Patched (2022-11-10 r83330)
Platform: x86_64-pc-linux-gnu (64-bit)
Running under: Debian GNU/Linux bookworm/sid

Matrix products: default
BLAS:   /usr/lib/x86_64-linux-gnu/openblas-serial/libblas.so.3
LAPACK: /usr/lib/x86_64-linux-gnu/openblas-serial/libopenblas-r0.3.21.so

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

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

other attached packages:
[1] readxl_1.4.1    saemix_3.2     npde_3.3       knitr_1.41
[5] mkin_1.2.2      rmarkdown_2.19 nvimcom_0.9-133

loaded via a namespace (and not attached):
 [1] highr_0.9        cellranger_1.1.0 compiler_4.2.2   pillar_1.8.1
 [5] tools_4.2.2      mclust_6.0.0     digest_0.6.31    evaluate_0.19
 [9] lifecycle_1.0.3  tibble_3.1.8     gtable_0.3.1     nlme_3.1-161
[13] lattice_0.20-45  pkgconfig_2.0.3  rlang_1.0.6      cli_3.5.0
[17] DBI_1.1.3        yaml_2.3.6       xfun_0.35        fastmap_1.1.0
[21] gridExtra_2.3    stringr_1.5.0    dplyr_1.0.10     generics_0.1.3
[25] vctrs_0.5.1      lmtest_0.9-40    grid_4.2.2       tidyselect_1.2.0
[29] inline_0.3.19    deSolve_1.34     glue_1.6.2       R6_2.5.1
[33] fansi_1.0.3      ggplot2_3.4.0    magrittr_2.0.3   codetools_0.2-18
[37] scales_1.2.1     htmltools_0.5.4  assertthat_0.2.1 colorspace_2.0-3
[41] utf8_1.2.2       stringi_1.7.8    munsell_0.5.0    zoo_1.8-11
```