Simulation suite - comparing results

Emmanuelle Comets

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Setup

Computational functions

Note to self: bias=mean(estimation errors)

- summary statistics
  - sample mean:
$$\bar{\theta} = \frac{1}{K}\sum_k \hat{\theta}_k$$
  - sample variance
$$S^2_\theta = var(\hat{\theta} - \bar{\theta}) = \frac{1}{K-1}\sum_k (\hat{\theta}_k - \bar{\theta})^2$$
- absolute metrics
  - absolute bias
    - defined as the difference
$$E(\hat{\theta}) - \theta_0$$
    - estimated as
$$\bar{\theta} - \theta_0$$
  - precision
    - defined as the variance of the estimates
$$E\left((\theta - E(\theta)\right)^2$$
    - estimated as
$$S^2_\theta$$
  - accuracy (MSE)
    - defined as
$$MSE = E((\theta - \theta_0)^2)$$
    - estimated as
$$\frac{1}{K}\sum_k (\hat{\theta}_k - \bar{\theta})^2$$
    - RMSE: square root of MSE
$$RMSE = \sqrt{MSE}$$
- relative Bias
  - defined as the relative difference from true parameter in simhelpers
$$E(\hat{\theta})/\theta$$

    * estimated as
    $$mean(\hat{\theta})/\theta_0$$
    * should be close to 1
  - here, we define it as the relative difference from true parameter minus 1
    $$E(\hat{\theta} - \theta)/\theta$$
    * estimated as
    $$mean(\hat{\theta} - \theta_0)/\theta_0$$
    * should be close to 0
- relative MSE
  - accuracy in relative terms
  - defined as
    $$E((\hat{\theta} - \theta)^2)/\theta^2$$
  - **approximated** as
    $$\left((\bar{\theta} - \theta_0)^2 + S_\theta^2\right)/\theta_0^2$$
  - take square root to obtain the relative RMSE

Note **TODO**: install simhelpers package for computation of these metrics + the MC error

Continuous data

Emax and Hill models

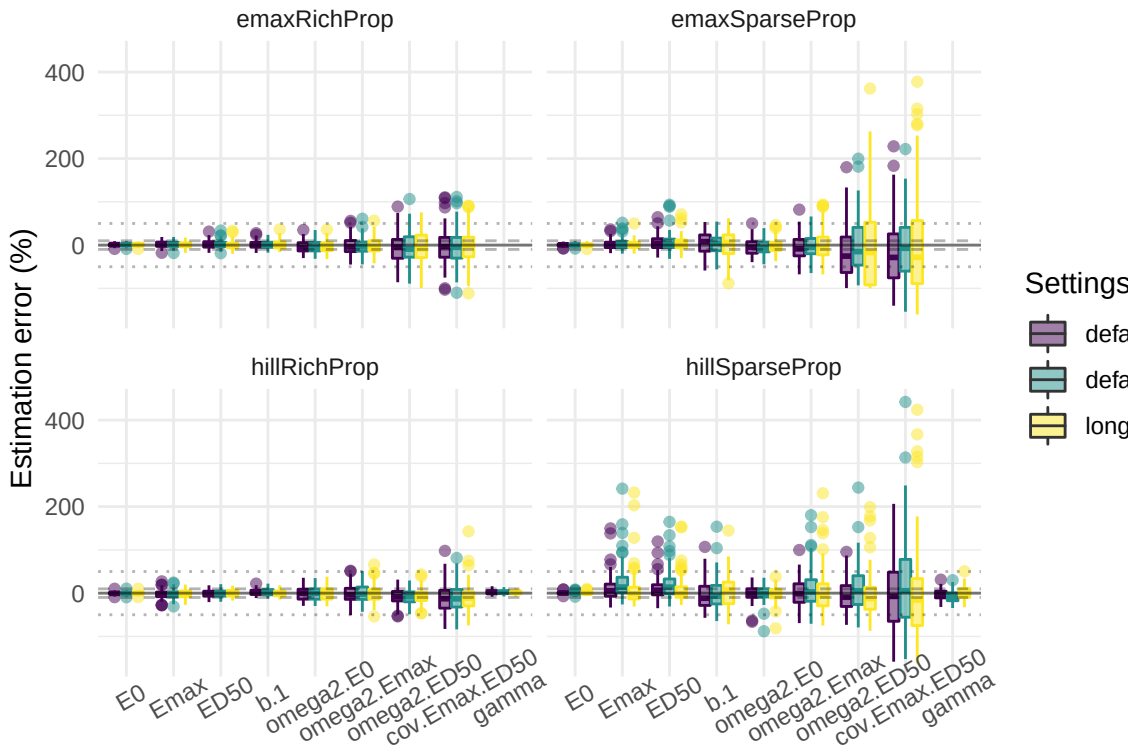
Data was simulated according to an Emax model or a Hill model (the first N=100 simulated datasets from the 200 simulated for the Pharm Res paper).

Settings

```
dataType <- "cont"
parpop<-c(5,30,500,3)
nampar<-c("E0","Emax","ED50","gamma")
omega<-diag(c(0.09,0.49,0.49))
omega[3,2]<-omega[2,3]<-0.245
respar<-c(0.1)
```

Simulation results

```
runDate <- '220913'
who <- "eco"
saemixVersion <-"cran31"
exampleName <- "doseResponsePlanProp"
runSettings <- c("defaultTrue","defaultFalse","longFalse")
runScenarios <- c("emaxRichProp","emaxSparseProp","hillRichProp","hillSparseProp")
```



Version 3.1 on CRAN

```
## pdf
##   2
```

Bias and accuracy of the estimates in the different settings and scenarios

% latex table generated in R 3.6.3 by xtable 1.8-4 package % Wed Sep 14 14:29:20 2022

% latex table generated in R 3.6.3 by xtable 1.8-4 package % Wed Sep 14 14:29:20 2022 \begin{table}[ht]

	param	true	bias	rrmse	bias	rrmse	bias	rrmse
1	emaxRichProp							
2	E0	5.00	0.84	0.12	0.90	0.12	0.78	0.12
3	Emax	30.00	1.61	0.53	1.82	0.53	0.66	0.53
4	ED50	500.00	1.79	0.89	2.26	0.92	0.18	0.91
5	b.1	0.10	0.86	0.75	0.93	0.76	1.45	1.12
6	omega2.E0	0.09	-3.24	1.81	-3.11	1.83	-3.14	1.86
7	omega2.Emax	0.49	-1.86	3.55	-2.25	3.32	-2.11	3.38
8	omega2.ED50	0.49	-3.86	11.36	-3.52	12.32	-6.20	15.66
9	cov.Emax.ED50	0.24	-3.19	15.34	-3.56	15.42	-4.29	16.27
10	emaxSparseProp							
11	E0	5.00	0.60	0.10	0.62	0.12	0.31	0.13
12	Emax	30.00	1.03	1.01	2.52	1.50	1.21	1.06
13	ED50	500.00	4.74	3.26	6.34	5.06	3.40	3.22
14	b.1	0.10	4.94	7.18	0.71	5.42	0.83	9.97
15	omega2.E0	0.09	-3.81	3.45	-4.15	2.94	-2.62	2.98
16	omega2.Emax	0.49	-6.22	7.60	-3.23	7.72	-0.15	12.29
17	omega2.ED50	0.49	-16.64	36.61	0.41	36.72	-0.85	102.73
18	cov.Emax.ED50	0.24	-21.36	58.87	-6.46	56.35	-0.22	137.87
19	hillRichProp							
20	E0	5.00	-0.42	0.12	-0.40	0.12	-0.38	0.12
21	Emax	30.00	-2.74	1.05	-2.66	1.03	-1.90	0.94
22	ED50	500.00	-1.07	0.73	-1.03	0.73	-0.04	0.70
23	gamma	3.00	2.35	0.31	2.29	0.28	1.45	0.23
24	b.1	0.10	1.87	0.59	2.26	0.63	-0.34	0.56
25	omega2.E0	0.09	-1.46	2.45	-1.70	2.49	-1.23	2.49
26	omega2.Emax	0.49	-1.27	3.79	-0.69	3.62	-0.25	3.70
27	omega2.ED50	0.49	-8.55	3.90	-8.25	3.73	-7.65	3.40
28	cov.Emax.ED50	0.24	-11.90	13.22	-10.98	12.75	-10.44	11.21
29	hillSparseProp							
30	E0	5.00	0.33	0.07	-0.18	0.07	0.47	0.08
31	Emax	30.00	11.91	10.49	24.72	22.79	7.81	15.43
32	ED50	500.00	10.63	6.69	22.44	16.46	7.07	8.99
33	gamma	3.00	-2.43	1.43	-7.90	2.39	0.64	2.25
34	b.1	0.10	-4.08	10.53	-0.55	11.32	4.95	12.80
35	omega2.E0	0.09	-0.02	2.83	-0.40	2.89	-1.60	2.74
36	omega2.Emax	0.49	0.96	9.61	8.62	20.69	1.69	23.27
37	omega2.ED50	0.49	-2.68	15.91	9.66	27.09	-4.74	27.71
38	cov.Emax.ED50	0.24	-2.46	65.36	20.21	106.51	-3.39	123.68

\caption{Relative bias and relative RMSE (in %) in the example doseResponsePlanProp for settings:defaultTrue, defaultFalse, longFalse} \end{table} % latex table generated in R 3.6.3 by xtable 1.8-4 package % Wed Sep 14 14:29:20 2022 \begin{table}[ht]

	param	empSE	bias	rrmse	bias	rrmse	bias	rrmse
1	emaxRichProp							
2	E0	0.17	-5.80	0.75	-5.56	0.73	-5.65	0.74
3	Emax	2.14	6.82	1.79	8.02	1.86	4.04	1.34
4	ED50	46.36	-5.67	2.84	-5.78	3.01	-10.77	3.91
5	b.1	0.01	-19.58	4.24	-20.16	4.47	-33.72	11.74
6	omega2.E0	0.01	16.69	4.70	15.90	4.44	15.28	4.22
7	omega2.Emax	0.09	-12.91	3.68	-9.85	2.97	-10.84	3.08
8	omega2.ED50	0.16	-34.20	13.69	-36.68	15.40	-44.38	21.35
9	cov.Emax.ED50	0.10	-21.09	6.53	-21.22	6.54	-24.00	7.63
10	emaxSparseProp							
11	E0	0.16	-7.32	1.03	-13.13	2.12	-18.42	3.81
12	Emax	3.00	-26.51	9.08	-36.51	15.45	-27.54	10.29
13	ED50	87.11	-28.47	11.06	-39.77	18.96	-30.24	12.80
14	b.1	0.03	-22.69	5.85	-11.70	2.15	-31.01	14.14
15	omega2.E0	0.02	-11.64	2.62	-4.94	1.50	-5.78	1.71
16	omega2.Emax	0.13	-27.48	9.84	-27.54	10.06	-43.19	20.72
17	omega2.ED50	0.29	-31.93	13.16	-30.55	12.38	-59.96	38.32
18	cov.Emax.ED50	0.18	-33.61	14.01	-31.39	12.85	-57.06	34.79
19	hillRichProp							
20	E0	0.17	-9.04	1.37	-9.51	1.46	-9.20	1.41
21	Emax	2.96	-18.12	5.33	-17.13	4.96	-13.58	3.90
22	ED50	42.47	-10.77	3.03	-10.60	2.97	-8.36	2.40
23	gamma	0.15	-22.38	6.29	-17.00	4.31	-17.10	4.33
24	b.1	0.01	-8.25	1.13	-10.28	1.51	-10.69	1.59
25	omega2.E0	0.01	-4.18	2.17	-4.93	2.25	-5.17	2.26
26	omega2.Emax	0.10	-16.48	5.24	-14.15	4.52	-14.52	4.59
27	omega2.ED50	0.09	-19.77	6.20	-17.95	5.50	-13.98	4.22
28	cov.Emax.ED50	0.08	-29.44	10.55	-28.24	9.85	-22.88	7.19
29	hillSparseProp							
30	E0	0.13	-5.50	0.67	-4.59	0.59	-7.96	1.03
31	Emax	9.03	-57.46	38.02	-59.52	42.87	-67.18	52.36
32	ED50	117.86	-42.27	23.08	-50.08	32.46	-53.97	36.29
33	gamma	0.35	-17.82	6.92	-35.08	15.66	-29.57	13.34
34	b.1	0.03	12.25	9.35	6.22	5.24	6.64	6.06
35	omega2.E0	0.02	-12.25	4.30	-11.92	4.30	-6.07	4.13
36	omega2.Emax	0.15	-25.12	13.01	-37.22	24.61	-52.23	33.13
37	omega2.ED50	0.19	-34.67	14.34	-42.05	21.44	-50.44	28.26
38	cov.Emax.ED50	0.20	-34.46	14.72	-40.24	21.55	-52.55	30.86

\caption{Relative bias and relative RMSE (in %) on SE estimated by linearisation, compared to the empirical SE, in the example doseResponsePlanProp for settings:defaultTrue, defaultFalse, longFalse} \end{table}

	param	true	bias	rmse	precision	bias	rmse	precision	bias	rmse	precision
1	emaxRichProp										
2	E0	5.00	0.04	0.17	0.17	0.04	0.17	0.17	0.04	0.17	0.17
3	Emax	30.00	0.48	2.18	2.14	0.55	2.17	2.11	0.20	2.17	2.17
4	ED50	500.00	8.97	46.99	46.36	11.32	47.84	46.71	0.89	47.55	47.78
5	b.1	0.10	0.00	0.01	0.01	0.00	0.01	0.01	0.00	0.01	0.01
6	omega2.E0	0.09	-0.00	0.01	0.01	-0.00	0.01	0.01	-0.00	0.01	0.01
7	omega2.Emax	0.49	-0.01	0.09	0.09	-0.01	0.09	0.09	-0.01	0.09	0.09
8	omega2.ED50	0.49	-0.02	0.16	0.16	-0.02	0.17	0.17	-0.03	0.19	0.19
9	cov.Emax.ED50	0.24	-0.01	0.10	0.10	-0.01	0.10	0.10	-0.01	0.10	0.10
10	emaxSparseProp										
11	E0	5.00	0.03	0.16	0.16	0.03	0.17	0.17	0.02	0.18	0.18
12	Emax	30.00	0.31	3.00	3.00	0.76	3.66	3.59	0.36	3.08	3.07
13	ED50	500.00	23.72	89.86	87.11	31.68	112.00	107.97	16.99	89.29	88.10
14	b.1	0.10	0.00	0.03	0.03	0.00	0.02	0.02	0.00	0.03	0.03
15	omega2.E0	0.09	-0.00	0.02	0.02	-0.00	0.02	0.01	-0.00	0.02	0.02
16	omega2.Emax	0.49	-0.03	0.13	0.13	-0.02	0.14	0.14	-0.00	0.17	0.17
17	omega2.ED50	0.49	-0.08	0.30	0.29	0.00	0.30	0.30	-0.00	0.49	0.50
18	cov.Emax.ED50	0.24	-0.05	0.19	0.18	-0.02	0.18	0.18	-0.00	0.29	0.29
19	hillRichProp										
20	E0	5.00	-0.02	0.17	0.17	-0.02	0.17	0.17	-0.02	0.17	0.17
21	Emax	30.00	-0.82	3.06	2.96	-0.80	3.03	2.94	-0.57	2.89	2.85
22	ED50	500.00	-5.33	42.59	42.47	-5.17	42.59	42.49	-0.22	41.73	41.94
23	gamma	3.00	0.07	0.17	0.15	0.07	0.16	0.14	0.04	0.14	0.14
24	b.1	0.10	0.00	0.01	0.01	0.00	0.01	0.01	-0.00	0.01	0.01
25	omega2.E0	0.09	-0.00	0.01	0.01	-0.00	0.01	0.01	-0.00	0.01	0.01
26	omega2.Emax	0.49	-0.01	0.09	0.10	-0.00	0.09	0.09	-0.00	0.09	0.09
27	omega2.ED50	0.49	-0.04	0.10	0.09	-0.04	0.09	0.09	-0.04	0.09	0.08
28	cov.Emax.ED50	0.24	-0.03	0.09	0.08	-0.03	0.09	0.08	-0.03	0.08	0.08
29	hillSparseProp										
30	E0	5.00	0.02	0.13	0.13	-0.01	0.13	0.13	0.02	0.14	0.14
31	Emax	30.00	3.57	9.67	9.03	7.42	14.27	12.25	2.34	11.73	11.55
32	ED50	500.00	53.14	128.75	117.86	112.22	202.14	168.98	35.34	149.22	145.70
33	gamma	3.00	-0.07	0.36	0.35	-0.24	0.46	0.40	0.02	0.45	0.45
34	b.1	0.10	-0.00	0.03	0.03	-0.00	0.03	0.03	0.00	0.04	0.04
35	omega2.E0	0.09	-0.00	0.02	0.02	-0.00	0.02	0.02	-0.00	0.01	0.01
36	omega2.Emax	0.49	0.00	0.15	0.15	0.04	0.22	0.22	0.01	0.24	0.24
37	omega2.ED50	0.49	-0.01	0.19	0.19	0.05	0.25	0.25	-0.02	0.26	0.26
38	cov.Emax.ED50	0.24	-0.01	0.20	0.20	0.05	0.25	0.25	-0.01	0.27	0.27

Table 1: Bias, precision and accurary in the example doseResponsePlanProp for settings:defaultTrue, defaultFalse, longFalse