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Insel Basic Pharmacokinetic Modeling Workshop 2022

12th January 2022, KEMRI (virtual event)

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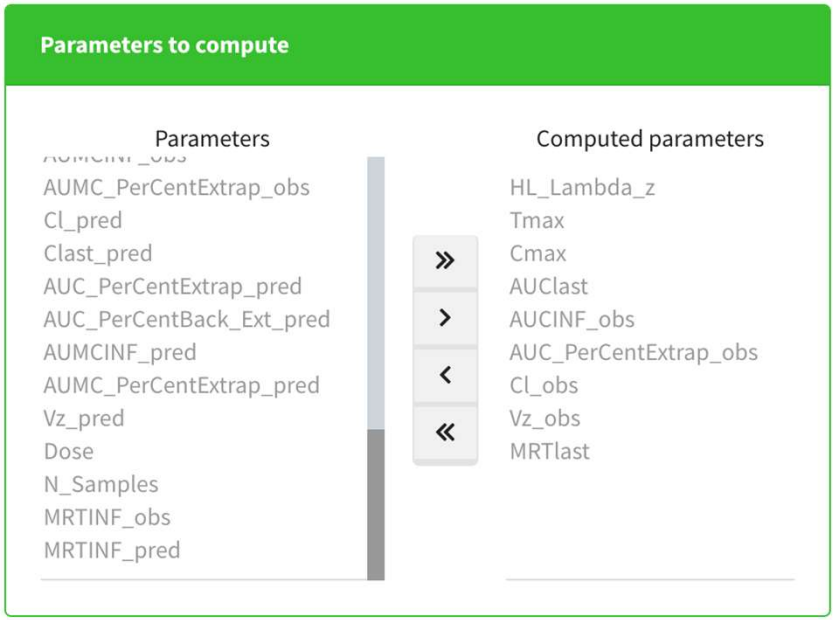
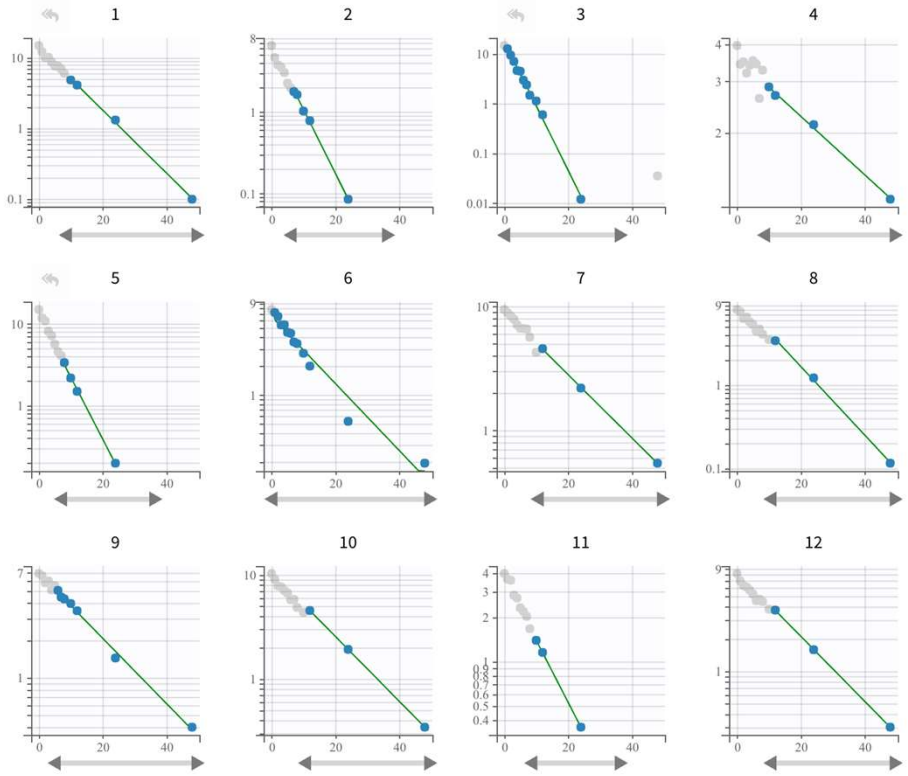
NCA hands-on exercises

Dataset_ee.csv

- Confirm dataset was imported properly
- Look at concentration curves to determine administration type
- Adjust lambda_z regression
- Select computed parameters
- Run and confirm validity / robustness
- Save your analysis as a project file



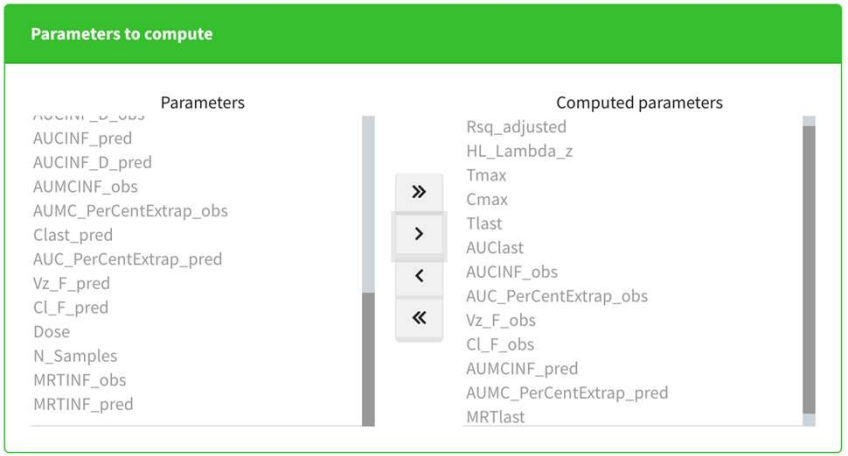
Dataset_ee.csv



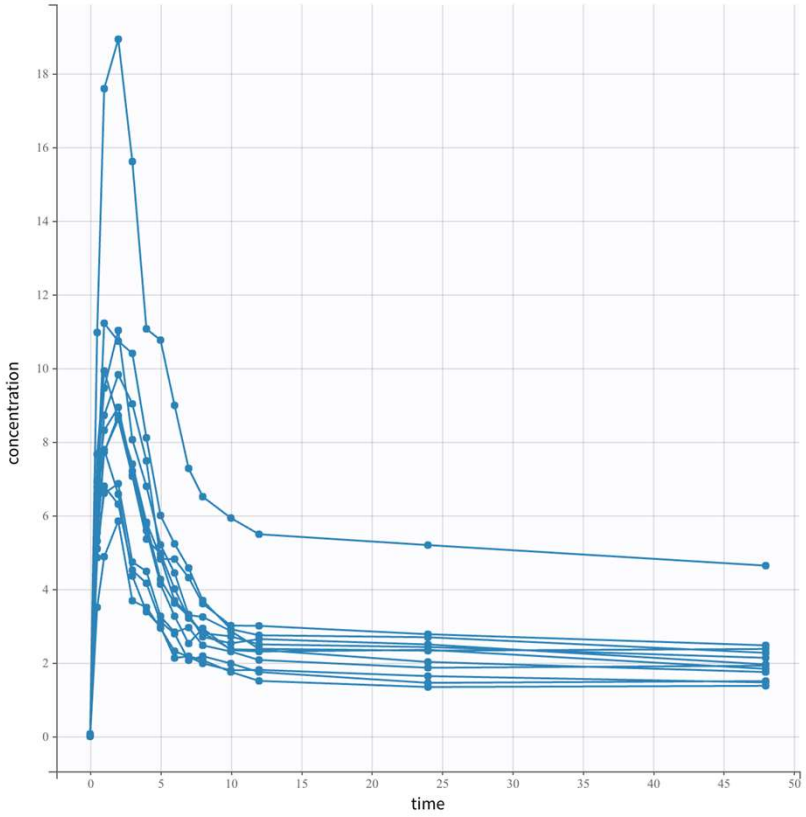
	MIN	Q1	MEDIAN	Q3	MAX	MEAN	SD
AUCINF_obs	33.46	67.45	106.14	136.71	157.4	99.88	42.86
AUC_%Extrap_obs	0.2	1.32	3.29	5.89	32.84	5.77	8.93
AUClast	33	66.18	101.61	121.97	145.3	92.66	37.45
Cl_obs	0.64	0.73	0.95	1.51	2.99	1.28	0.77
Cmax	3.96	6.69	8.08	12.46	14.89	9.11	3.9
HL_Lambda_z	2.32	5.36	7.97	10.7	30.22	9.42	7.21
MRTlast	3.91	6.47	10.62	13.33	19.65	10.5	4.53
Tmax	0	0	0	0	0	0	0
Vz_obs	5.77	8.69	11.76	16.34	27.7	13.8	7

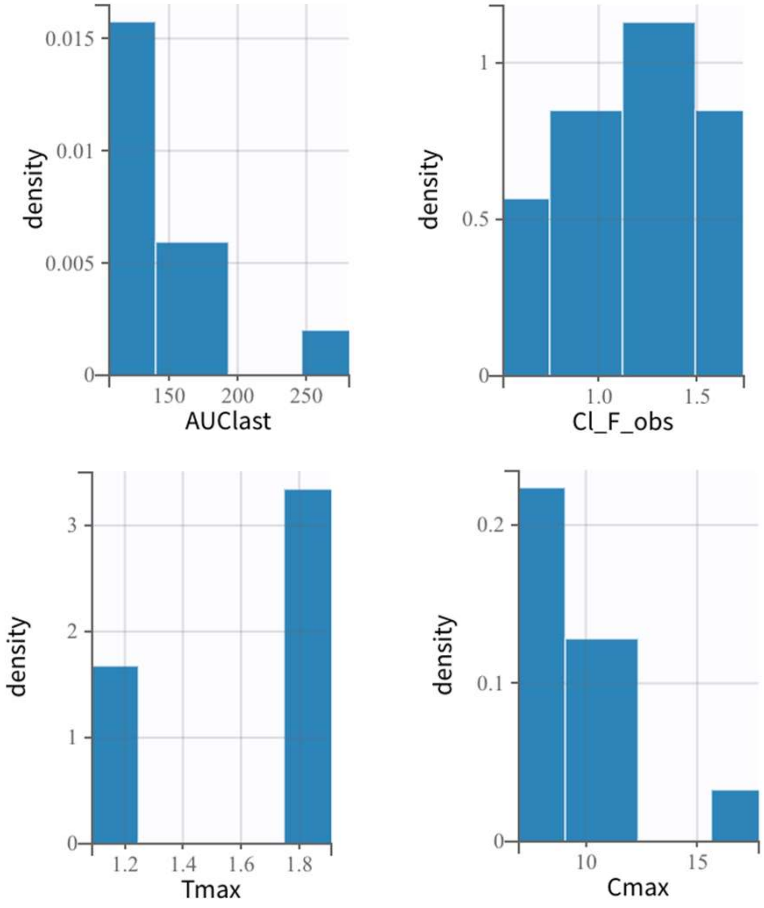
Dataset_allo.csv

- Confirm dataset was imported properly
- Look at concentration curves to determine administration type
- Adjust lambda_z regression
- Select computed parameters
- Run and confirm validity / robustness
- **Compute $AUC_{0\text{-}12h}$**
- Save your analysis as a project file

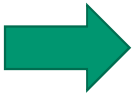


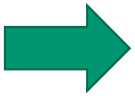
Dataset_allo.csv





Dataset_allo.csv

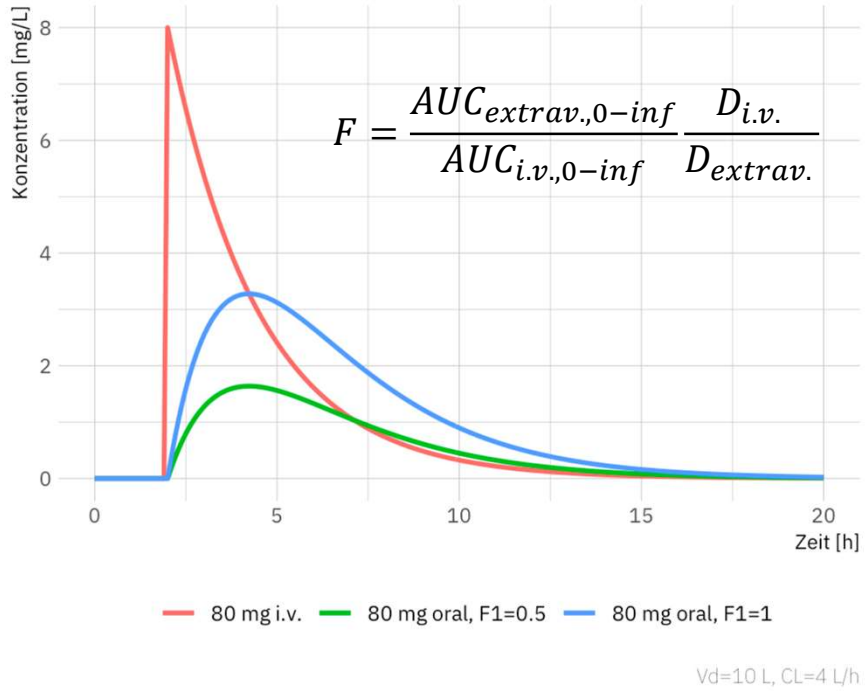




	MIN	Q1	MEDIAN	Q3	MAX	MEAN	SD	SE	CV
AUCINF_obs	267.57	319.41	393.28	620.44	1288.24	532.94	317.72	91.72	59.62
AUC_0_12	34.13	41.13	53.4	63.12	118.16	57.15	22.24	6.42	38.92
AUC_0_12_D	0.068	0.082	0.11	0.13	0.24	0.11	0.044	0.013	38.92
AUC_0_24	54.79	62.53	82.01	94.56	182.26	86.7	34.23	9.88	39.47
AUC_0_24_D	0.11	0.13	0.16	0.19	0.36	0.17	0.068	0.02	39.47
AUC_%Extrap_obs	61.67	64.35	69.44	75.54	85.37	70.58	7.19	2.07	10.18
AUClast	87.85	103	134.32	154.24	300.13	140.9	56.35	16.27	39.99
AUMCINF_pred	26533.1	35298.09	62718.45	122365.41	343981.38	102461.14	101313.6	29246.72	98.88
AUMC_%Extrap_pred	91.43	93.87	96.24	97.49	99.18	95.73	2.29	0.66	2.39
Cl_F_obs	0.39	0.81	1.28	1.57	1.87	1.19	0.5	0.14	42.31
Cmax	5.85	7.32	8.82	10.47	18.93	9.54	3.39	0.98	35.59
HL_Lambda_z	67.36	83.44	112.58	139.59	250.03	119.81	49.52	14.29	41.33
MRTlast	18.61	19	19.28	19.8	20.31	19.42	0.57	0.16	2.92
Rsq_adjusted	-0.12	0.5	0.94	0.96	1	0.73	0.36	0.1	49.11
Tlast	48	48	48	48	48	48	0	0	0
Tmax	1	1	2	2	2	1.67	0.49	0.14	29.54
Vz_F_obs	82.7	155.91	180.48	202.31	252.87	179.32	45.4	13.11	25.32

Bioavailability

- Crossover design
- Datasets:
  - IV_NOCOV_DTA.csv
  - ORAL_NOCOV_DTA.csv
- Look at and perform NCAs on both datasets
- You can use the mean of AUCINF_obs
- More informative: use a spreadsheet or R to calculate from individual estimates



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Bioavailability

	MIN	Q1	MEDIAN	Q3	MAX	MEAN	SD	SE	CV
AUCINF_obs	55.82	81.69	103.55	118.81	127.67	98.24	24.16	6.97	24.59
AUC_%Extrap_obs	0.056	0.96	3.94	6.36	17.02	4.56	4.68	1.35	102.58
AUClast	55.79	81.05	98.25	109.82	115.24	93.01	20.31	5.86	21.83
Cl_obs	0.59	0.63	0.73	0.92	1.34	0.82	0.25	0.071	30.09
Cmax	5	6.23	6.86	8.18	9.33	7.03	1.37	0.39	19.43
HL_Lambda_z	4.45	6.77	10.15	11.62	18.95	9.85	3.93	1.14	39.95
MRTlast	8.68	10.05	12.73	14.04	17.22	12.42	2.59	0.75	20.89
Tmax	0	0	0	0	1	0.083	0.29	0.083	346.41
Vz_obs	6.63	8.72	10.34	12.54	16.06	10.68	2.6	0.75	24.35

	MIN	Q1	MEDIAN	Q3	MAX	MEAN	SD	SE	CV
AUCINF_obs	36.63	44.95	53.93	55.46	58	50.11	7.21	2.08	14.39
AUC_%Extrap_obs	0.9	1.25	2.34	5.27	12.71	3.6	3.48	1	96.69
AUClast	36.16	43.38	49.28	53.68	56.69	48.24	6.74	1.94	13.97
Cl_F_obs	1.72	1.8	1.85	2.23	2.73	2.04	0.33	0.095	16.21
Cmax	2.1	2.42	2.71	3.07	4.32	2.85	0.62	0.18	21.58
HL_Lambda_z	6.81	7.33	8.3	10.67	14.65	9.05	2.37	0.68	26.19
MRTlast	11.43	12.91	13.33	14.8	16.29	13.66	1.42	0.41	10.42
Tmax	3	4	4	5	7	4.42	1.08	0.31	24.53
Vz_F_obs	18.1	21.26	25.4	29.34	39.45	26.27	6.38	1.84	24.28

i.v. oral

$$F = \frac{AUC_{extrav.,0-inf}}{AUC_{i.v.,0-inf}} \frac{D_{i.v.}}{D_{extrav.}} = \frac{50.11}{98.24} \frac{75}{100} = 0.38$$

Bioavailability

D2 =B2/C2*75/100

	A	B	C	D
1	id	AUCINF_obs_oral	AUCINF_obs_iv	F1
2	1	54.29	117.22	0.347
3	2	36.63	55.82	0.492
4	3	44.36	76.85	0.433
5	4	58	127.67	0.341
6	5	45.54	86.67	0.394
7	6	53.56	91.09	0.441
8	7	55.34	124.08	0.335
9	8	47.08	97.45	0.362
10	9	55.57	109.64	0.380
11	10	56.51	120.39	0.352
12	11	39.44	61.96	0.477
13	12	54.95	110.14	0.374
14				
15				
16			mean	0.394
17			SD	0.054
18			SEM	0.016