Pmetrics Objects and Plots

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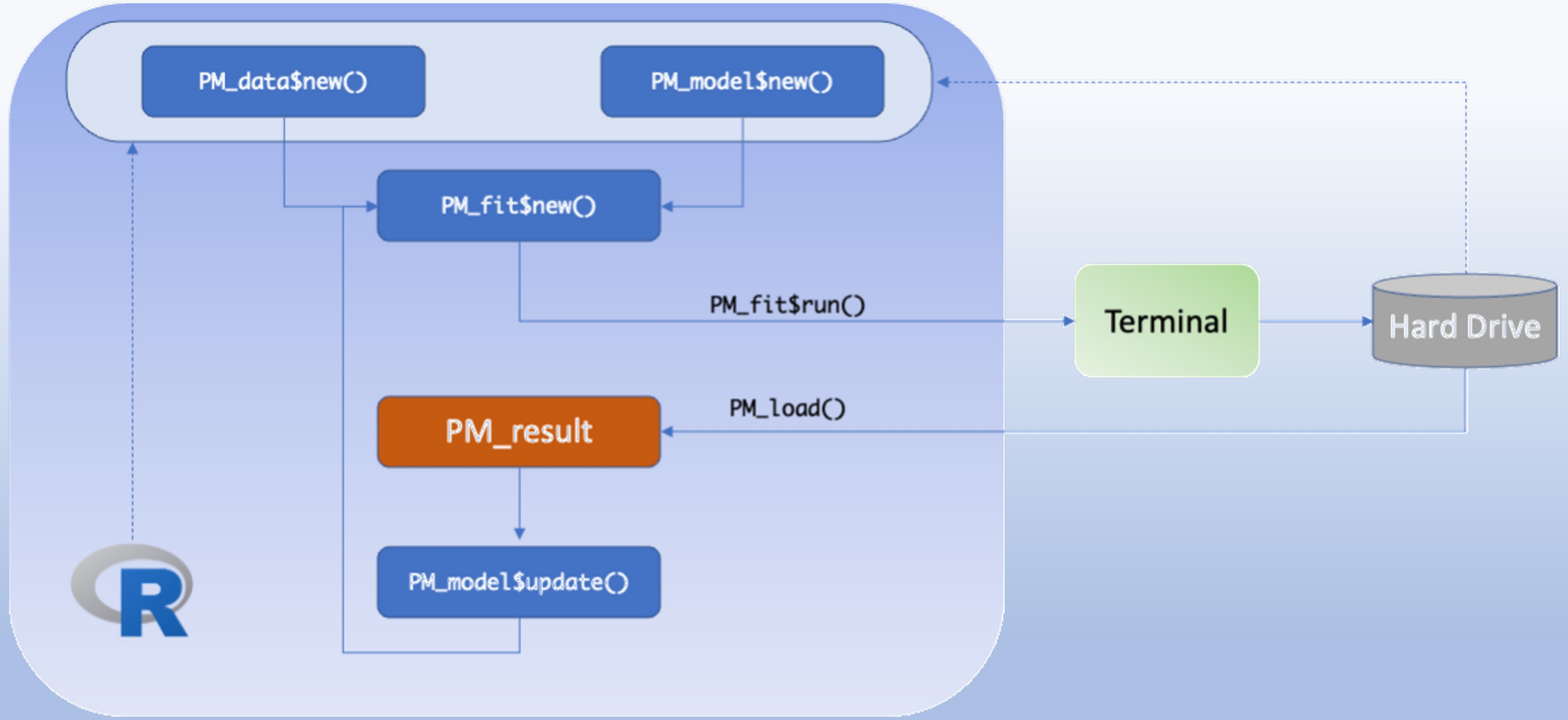
General Workflow



General Workflow

1. After a run is complete an HTML summary page is created and displayed
2. A sequentially numbered run folder is created
3. The results can be loaded into R with `PM_load(n)`, where `n` is the run number

PM_result

- A PM_result object is created by PM_load(1) after NPAG/IT2B run 1, with the following fields
  - op
  - final
  - cycle
  - cov
  - pop and post (NPAG only)
  - data
  - model
  - Npdata/ITdata

PMop objects

- Observed vs. Predicted
- class: PMop, data.frame
- methods: plot, summary
- examples: run1$op, run2$op

PMop Structure

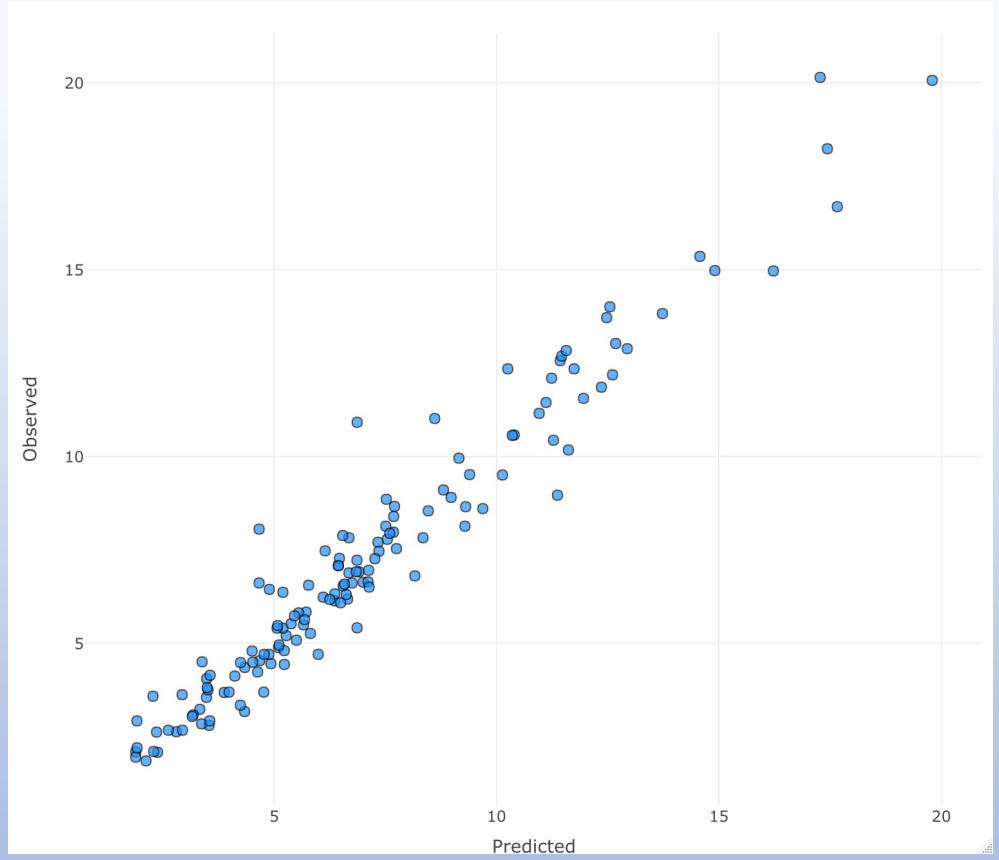
- Data frame with the following columns
  - **id**: Subject ID
  - **time**: time of observation/prediction
  - **obs**: the observed output value
  - **pred**: the predicted output value
  - **pred.type**: type of prediction, population or posterior
  - **icen**: summary of parameter distribution used for prediction, mean or median
  - **outeq**: output equation number for the observation/prediction
  - **block**: dosing block defined by EVID=4 events
  - **outSD**: SD of the observation, based on C0, C1, C2, C3 and gamma/lambda
  - **d**: pred-obs
  - **ds**: (pred-obs)^2
  - **wd**: (pred-obs)/SD
  - **wds** (pred-obs)^2 / SD^2

Summarizing PMop

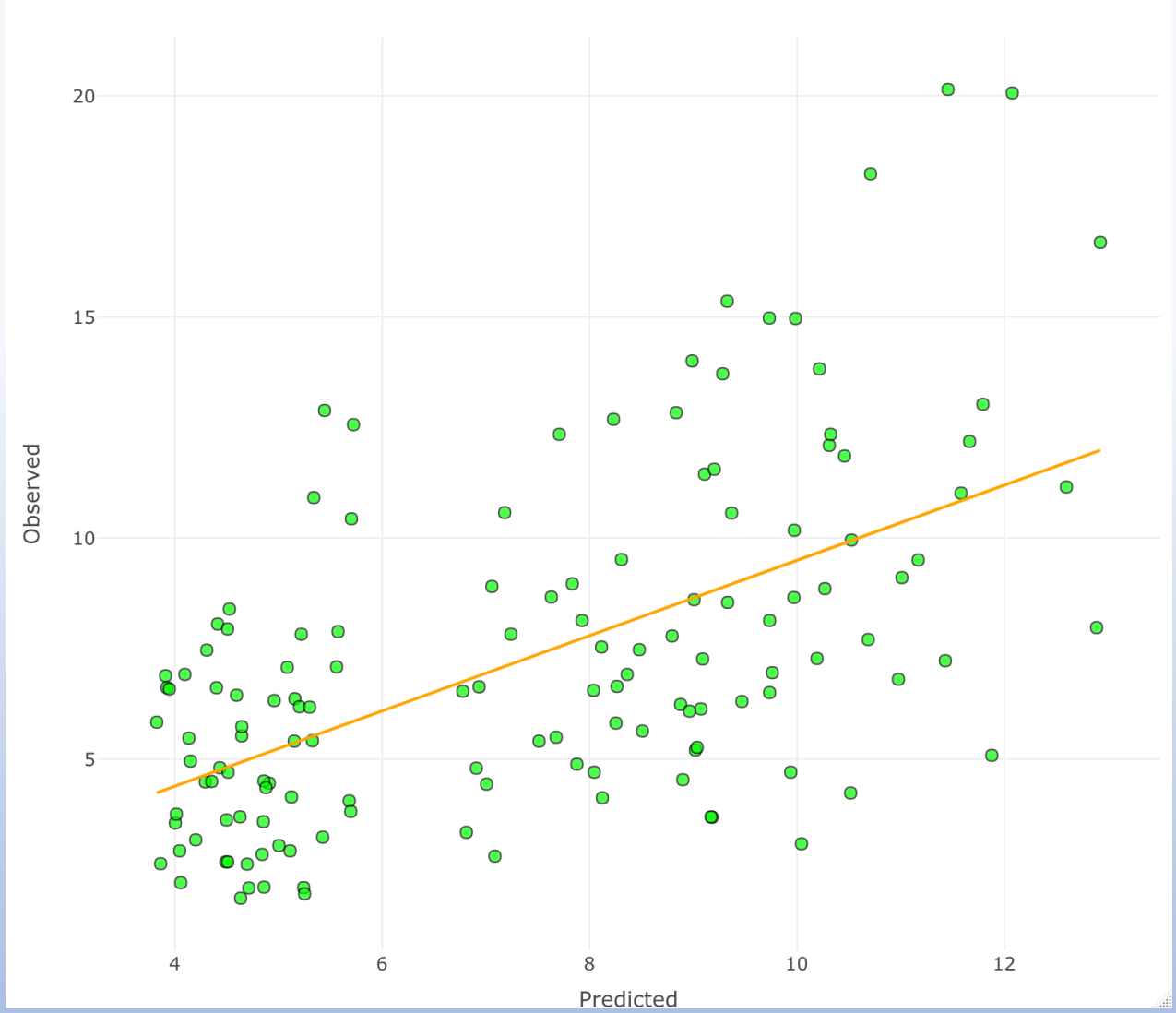
```
          Time   Obs  Pred
Min     120.00  1.86  1.96
25%     121.03  4.50  4.49
Median 126.00  6.56  6.61
75%     132.00  8.88  8.94
Max     144.98 20.15 20.39
Mean    127.69  7.24  7.09
SD        7.86  3.80  3.69


Mean prediction error: -0.1474
Mean weighted prediction error (bias): -0.0879 (P=0.9121 different than 0)
Mean squared prediction error: 0.7778
Root mean squared error (RMSE): 0.8819
Percent root mean squared error (%RMSE): 12.18
Mean weighed squared prediction error: 0.9965
Bias-adjusted mean squared prediction error: 0.7561
Bias-adjusted mean weighted squared prediction error (imprecision): 0.9888
```

```
run1$op$summary(pred.type="post", icen="median", outeq=1)
```

Plotting PMop




```
run1$op$plot()
```




```
run1$op$plot(pred.type="pop", marker = list(color = "green"), linear = T)
```

PMfinal objects

- Final cycle parameter values
- class: PMfinal, NPAG/IT2B, list
- methods: plot, summary
- examples: run1$final, run2$final

PMfinal Structure

- List with the following objects
  - **popPoints**: (NPAG only) Data frame of the final cycle grid points with column names equal to the name of each random parameter plus prob for the associated probability of that point
  - **popMean**: The final cycle mean for each random parameter distribution
  - **popSD**: The final cycle SD for each random parameter distribution
  - **popCV**: The final cycle coefZicient of variation for each random parameter distribution
  - **popVar**: The final cycle variance for each random parameter distribution
  - **popCov**: The final cycle covariance matrix for each random parameter distribution
  - **popCor**: The final cycle correlation matrix for each random parameter distribution
  - **popMedian**: The final cycle median for each random parameter distribution
  - **gridpts**: (NPAG only) The initial number of support points
  - **ab**: Matrix of boundaries for random parameter values. For NPAG, this is specified by the user prior to the run; for IT2B, it is calculated as a user specified multiple of the SD for the parameter value distribution
  - **postPoints**: (NPAG only) Data frame of the Bayesian posterior parameter points for each of the first 100 subjects, with the columns **id**, subject ID; **point**, point number for that subject; **parameters**, parameters in the model; **prob**, probability of each point in the posterior for each patient

Summarizing PMfinal

	par	type	quantile	value
1	Ka	WtMed	0.025	4.608512e-01
2	Ka	WtMed	0.500	6.625952e-01
3	Ka	WtMed	0.975	8.958512e-01
4	Ka	MAWD	0.025	4.092800e-03
5	Ka	MAWD	0.500	1.498528e-01
6	Ka	MAWD	0.975	3.180688e-01
7	Ke	WtMed	0.025	3.519846e-02
8	Ke	WtMed	0.500	4.393907e-02
9	Ke	WtMed	0.975	6.755382e-02
10	Ke	MAWD	0.025	4.409361e-03
11	Ke	MAWD	0.500	1.369061e-02
12	Ke	MAWD	0.975	2.131143e-02
13	V	WtMed	0.025	6.287781e+01
14	V	WtMed	0.500	7.339845e+01
15	V	WtMed	0.975	1.018518e+02
16	V	MAWD	0.025	5.888538e+00
17	V	MAWD	0.500	2.025000e+01
18	V	MAWD	0.975	3.817413e+01
19	Tlag1	WtMed	0.025	6.866592e-01
20	Tlag1	WtMed	0.500	1.177336e+00
21	Tlag1	WtMed	0.975	1.791292e+00
22	Tlag1	MAWD	0.025	1.992990e-01
23	Tlag1	MAWD	0.500	4.906768e-01
24	Tlag1	MAWD	0.975	8.750000e-01

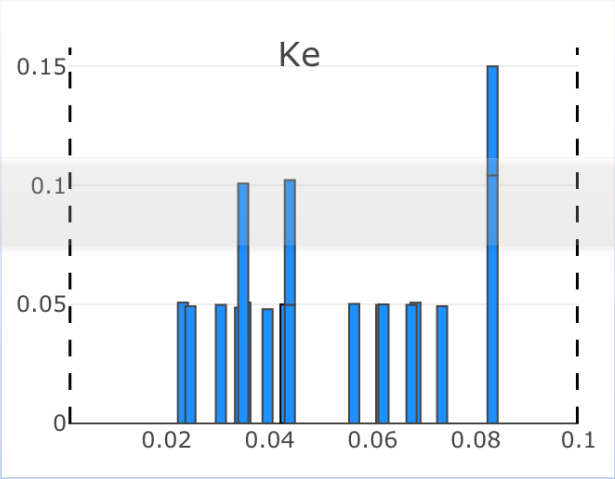
NPAG

	mean	se.mean	cv.mean	var	se.var
Ka	1.3579700	0.137701091	0.10140216	3.792318e-01	1.230390e-01
Ke	0.0444298	0.003619635	0.08146863	2.620352e-04	8.501543e-05
V0	88.8163000	8.490104143	0.09559173	1.441637e+03	4.677289e+02
Tlag1	1.6135400	0.084027186	0.05207630	1.412114e-01	4.581501e-02

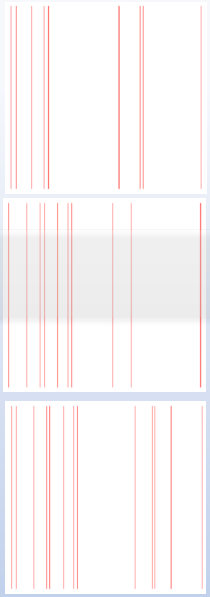
IT2B

```
run1$final$summary(lower = 0.025, upper = 0.975) #NPAG
run1$final$summary() #IT2B
```

Confidence in NP



17 points



1000 sets
x
17 points

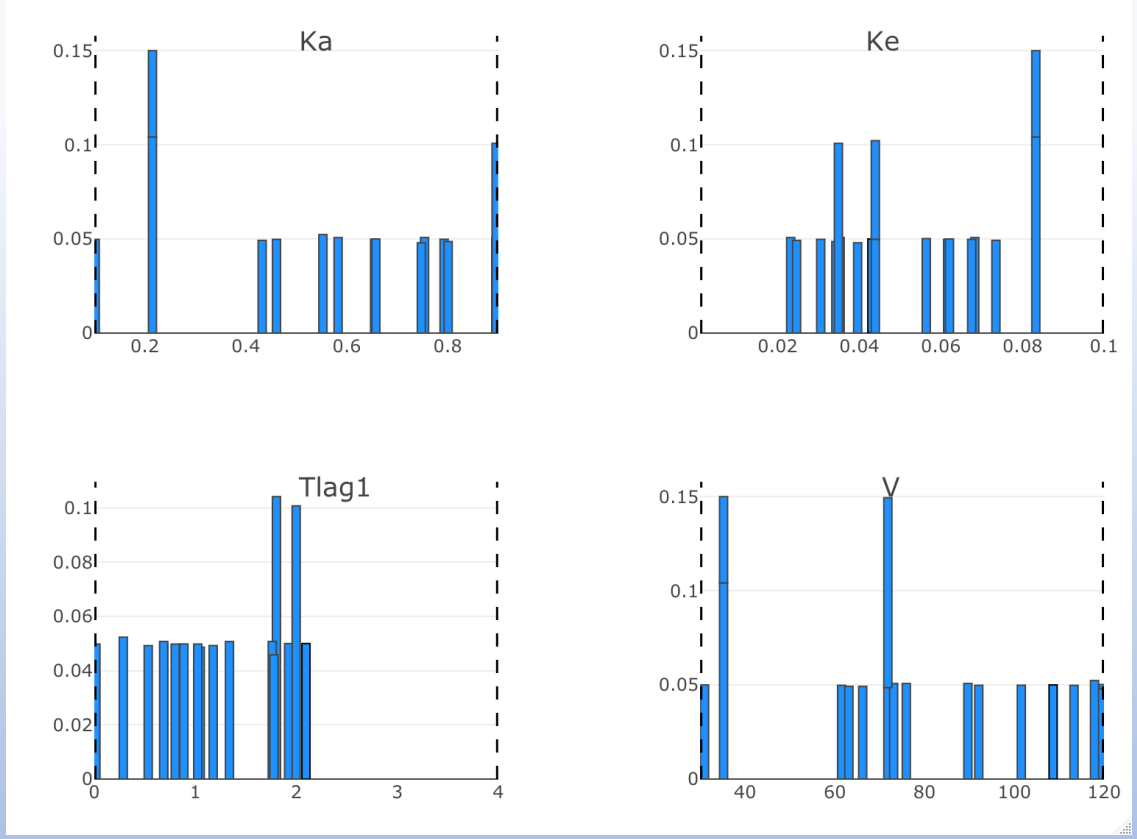
1000
medians
MADs

Median (2.5%, 97.5%)
MAWD (2.5%, 97.5%)

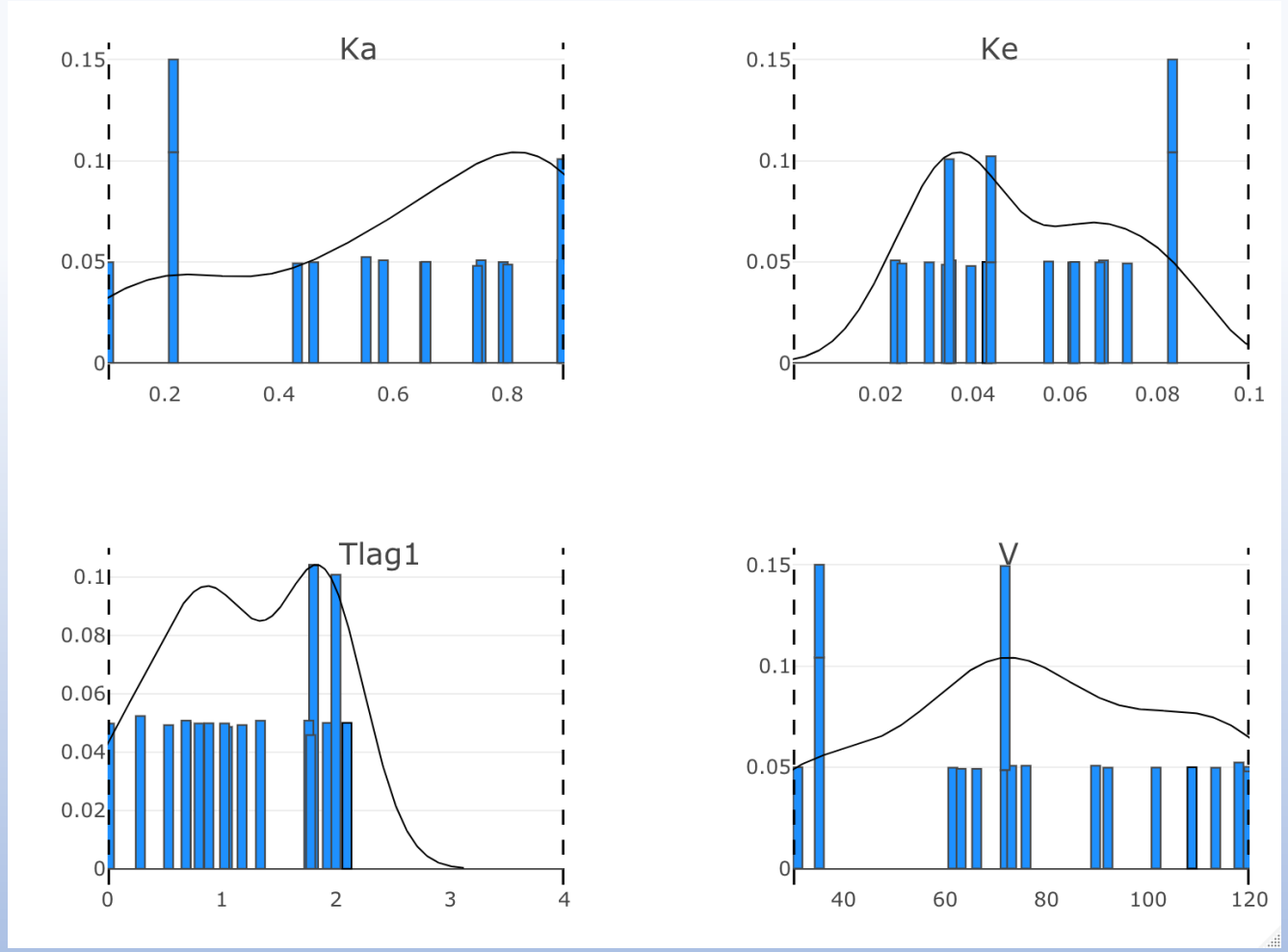
Parametric Confidence

- SE (mean) = SD/sqrt(nsub)
- SE (var) = var * sqrt(2/(nsub-1))

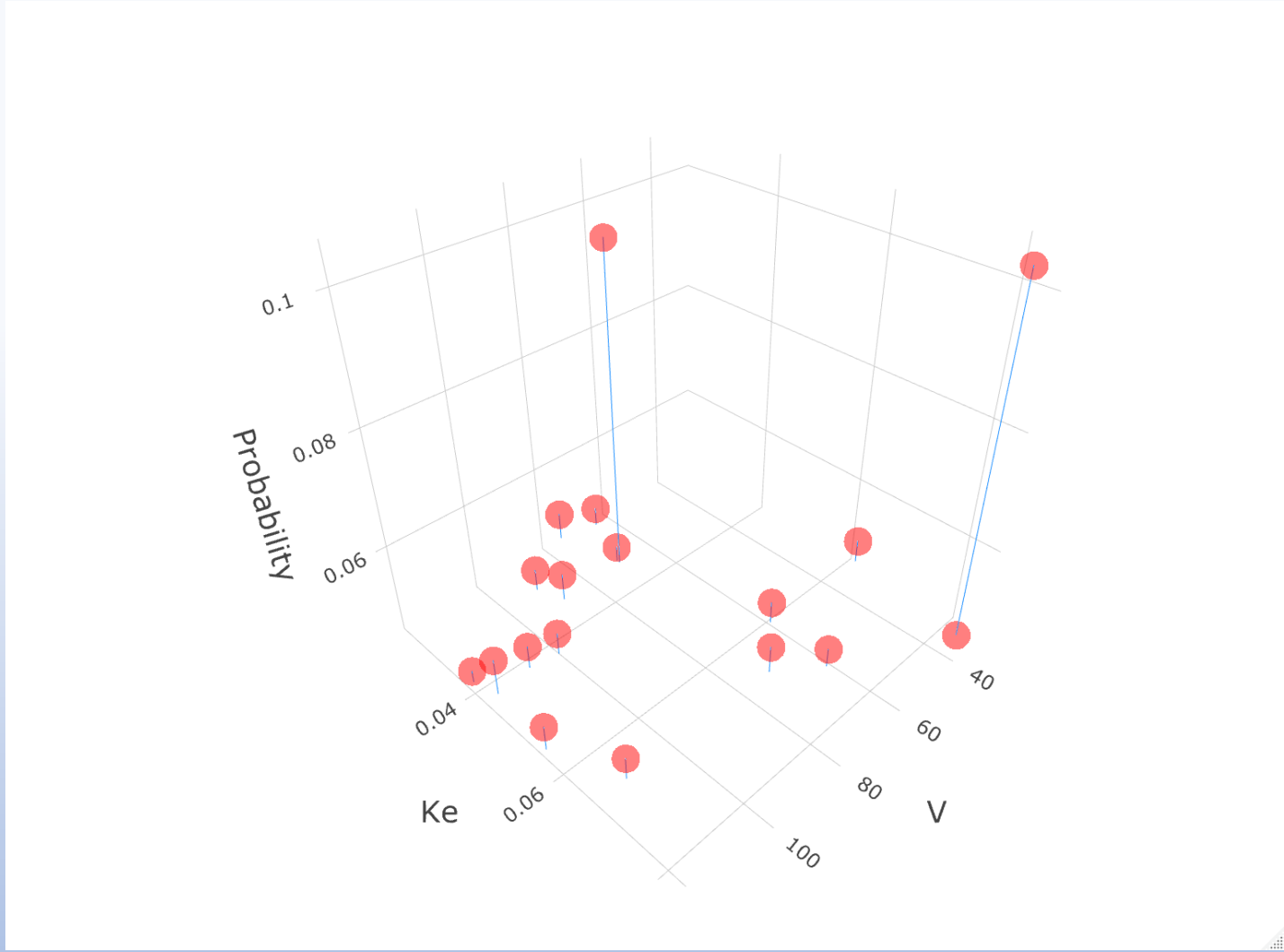
Plot PMfinal



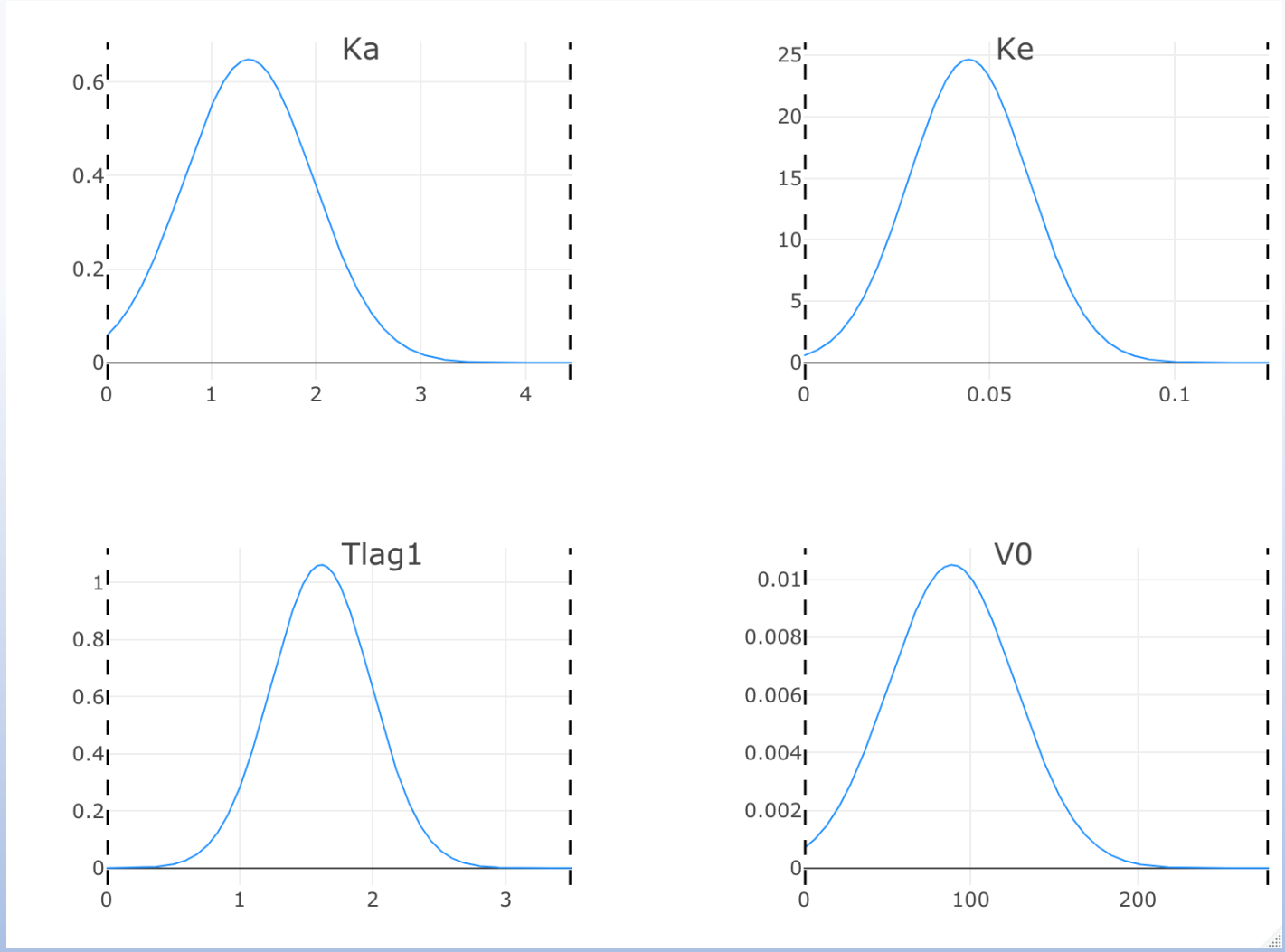

```
run1$final$plot()
```



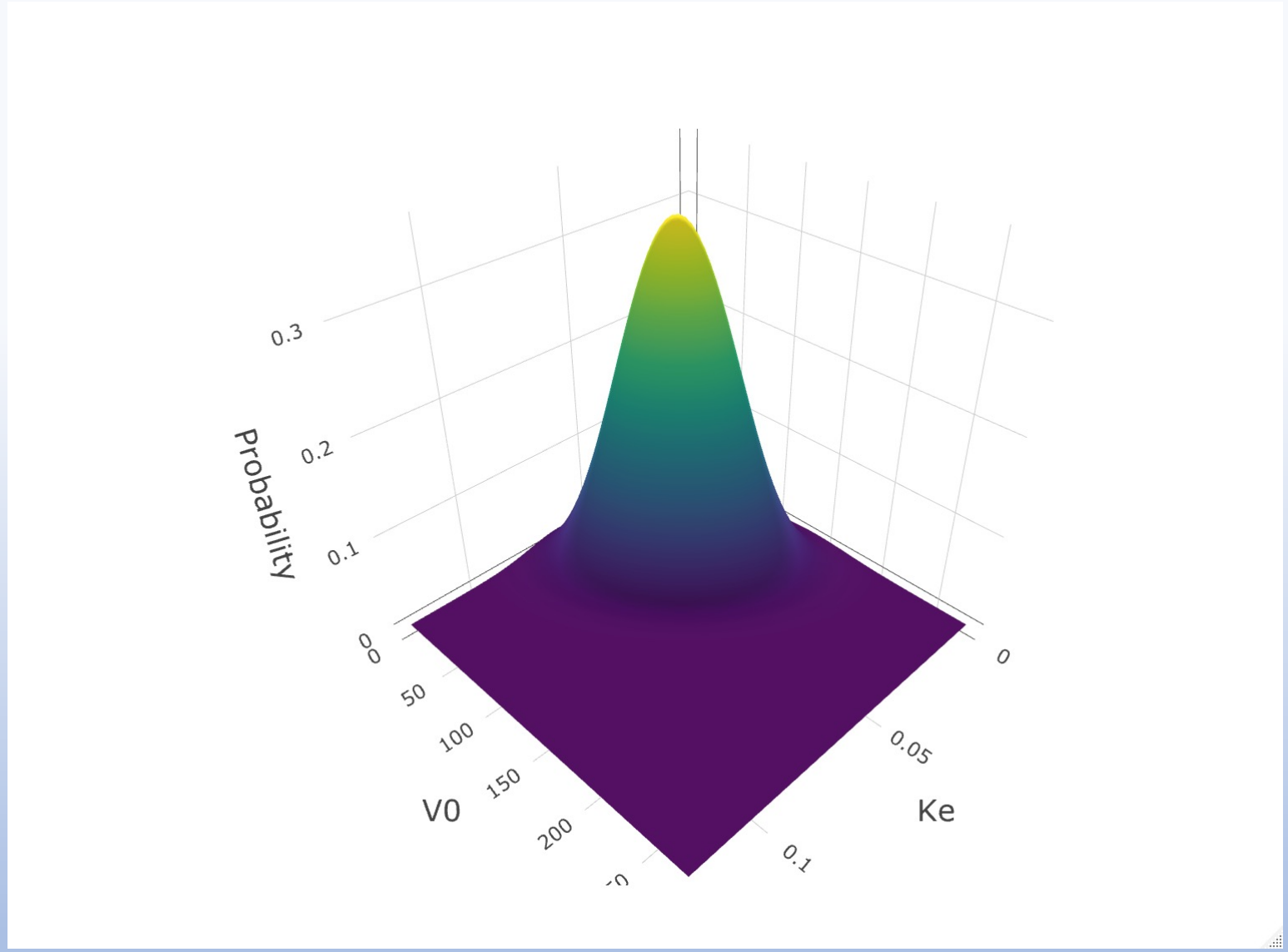

```
run1$final$plot(density=T)
```




```
run1$final$plot(Ke~V)
```




```
run2$final$plot()
```



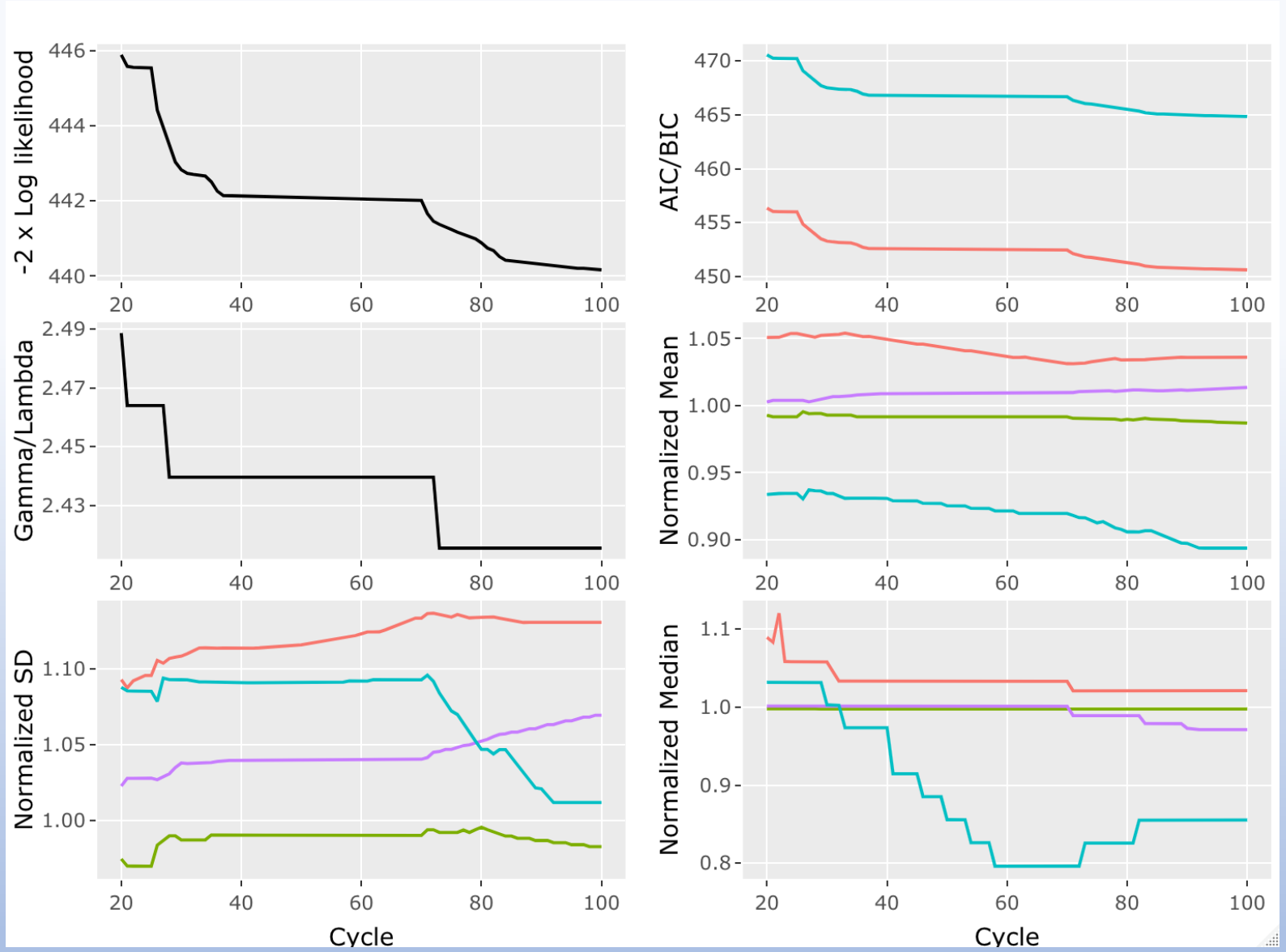

```
run2$final$plot(Ke~V0)
```

PMcycle objects

- Cycle log-likelihoods, gamma/lambda, AIC, BIC, normalized parameter means, medians, SD
- class: PMcycle, list
- methods: plot
- examples: run1$cycle, run2$cycle

PMcycle structure

- List with the following objects
  - **names** Vector of names of the random parameters
  - **cycnum** Vector cycle numbers, which may start at numbers greater than 1 if a non-uniform prior was specified for the run (NPAG only)
  - **ll** Matrix of cycle number and -2*Log-likelihood at each cycle
  - **gamlam** A matrix of cycle number and gamma or lambda at each cycle
  - **mean** A matrix of cycle number and the mean of each random parameter at each cycle, normalized to initial mean
  - **sd** A matrix of cycle number and the standard deviation of each random parameter at each cycle, normalized to initial standard deviation
  - **median** A matrix of cycle number and the median of each random parameter at each cycle, normalized to initial median
  - **aic** A matrix of cycle number and Akaike Information Criterion at each cycle
  - **bic** A matrix of cycle number and Bayesian (Schwartz) Information Criterion at each cycle




```
run1$cycle$plot()
```

PMcov objects

- Covariate values for each subject at each time of a covariate entry in the data file, combined with mean and median Bayesian posterior parameter estimates to enable covariate analysis
- class: PMcov, data.frame
- methods: plot, summary
- examples: run1$cov, run2$cov

PMcov structure

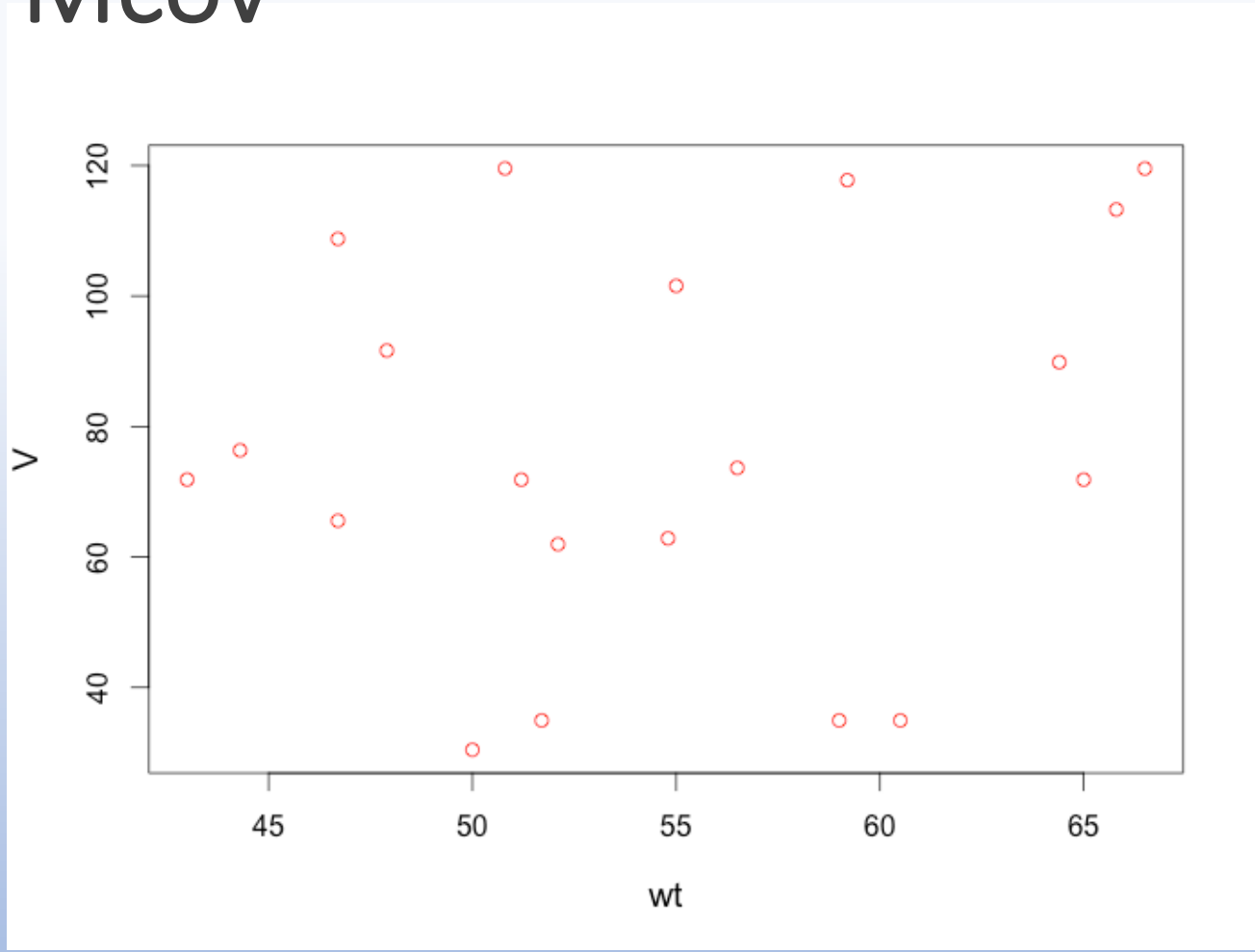
- **id** Subject identification
- **time** Times of covariate observations
- **covnames…** Columns with each covariate observations in the dataset for each subject and time
- **parnames…** Columns with each parameter in the model and the icen summary for each subject, replicated as necessary for covariate observation times and duplicated for Bayesian parameter means and medians
- **icen** The type of summarized Bayesian posterior individual parameter values: mean or median.

Summarizing PMcov

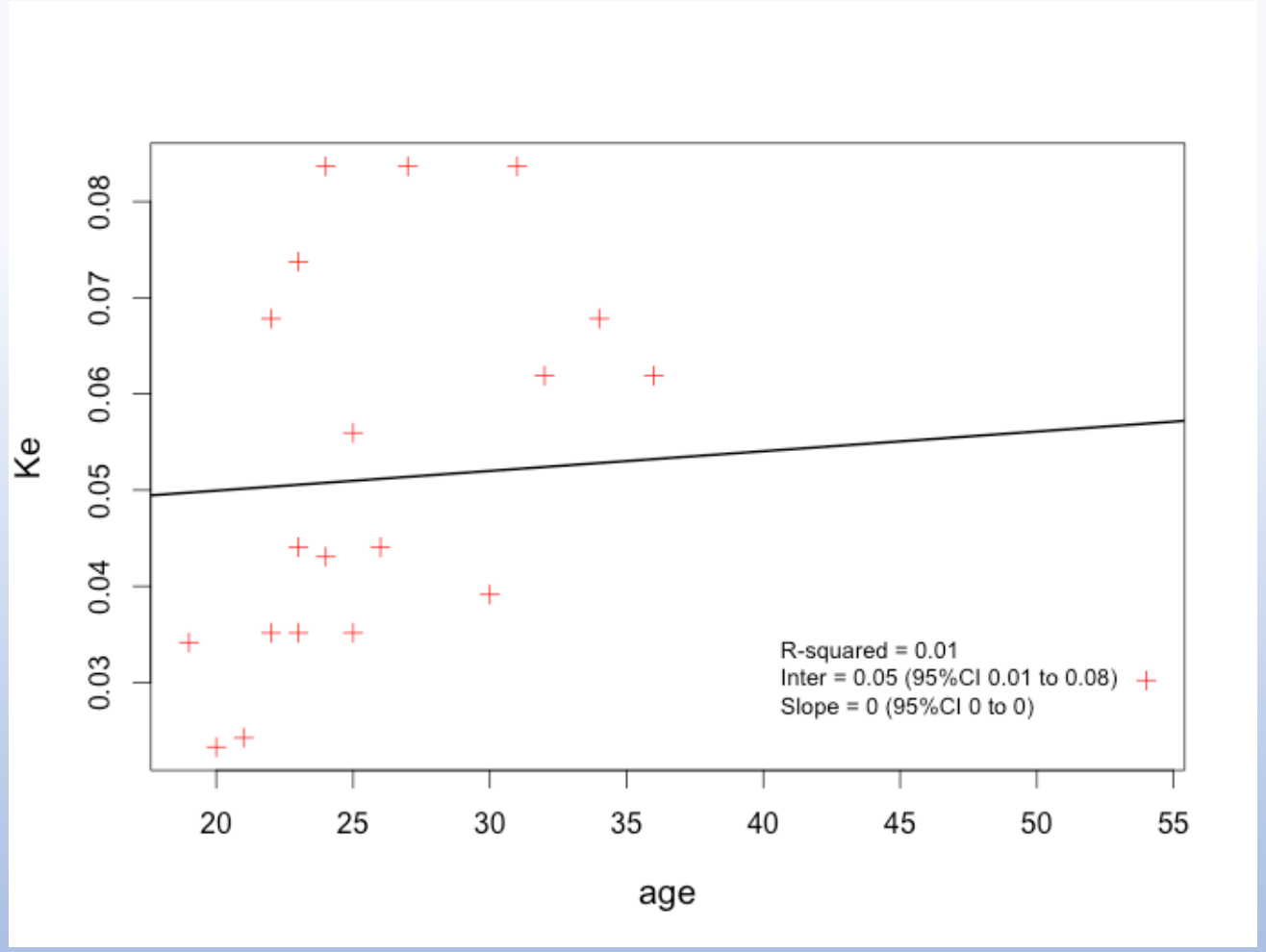
	id	time	wt	africa	age	gender	height	Ka	Ke	V	Tlag1
1	1	48	46.7	1	21	1	160	0.4320615	0.02425739	65.55692	0.54030745
2	2	60	66.5	1	30	1	174	0.7438166	0.03913897	119.52821	0.02096844
3	3	60	46.7	1	24	0	164	0.8960000	0.04307500	108.75000	2.10000000
4	4	60	50.8	1	25	1	165	0.8959996	0.05594505	119.54995	0.65999780
5	5	60	65.8	1	22	1	181	0.1040152	0.06782312	113.25171	0.02007594
6	6	60	65.0	1	23	1	177	0.8959928	0.03515412	71.85080	1.97996420
7	7	60	51.7	1	27	0	161	0.2160000	0.08366500	34.95000	1.78000000
8	8	60	51.2	1	22	1	163	0.8959970	0.03515467	71.85030	1.97998490
9	9	60	55.0	1	23	1	174	0.7919426	0.04406498	101.55640	0.89971335
10	10	60	52.1	1	32	1	163	0.6560146	0.06188319	61.95165	0.82007268
11	11	60	56.5	1	34	1	165	0.5840032	0.06782538	73.64966	1.33998410
12	12	60	47.9	1	54	0	160	0.4641038	0.03021784	91.63832	1.01995260
13	13	60	60.5	1	24	1	180	0.2160000	0.08366500	34.95000	1.78000000
14	14	60	59.3	1	36	1	174	0.5760553	0.04406031	117.75235	0.33989576

```
run1$cov$summary()
```

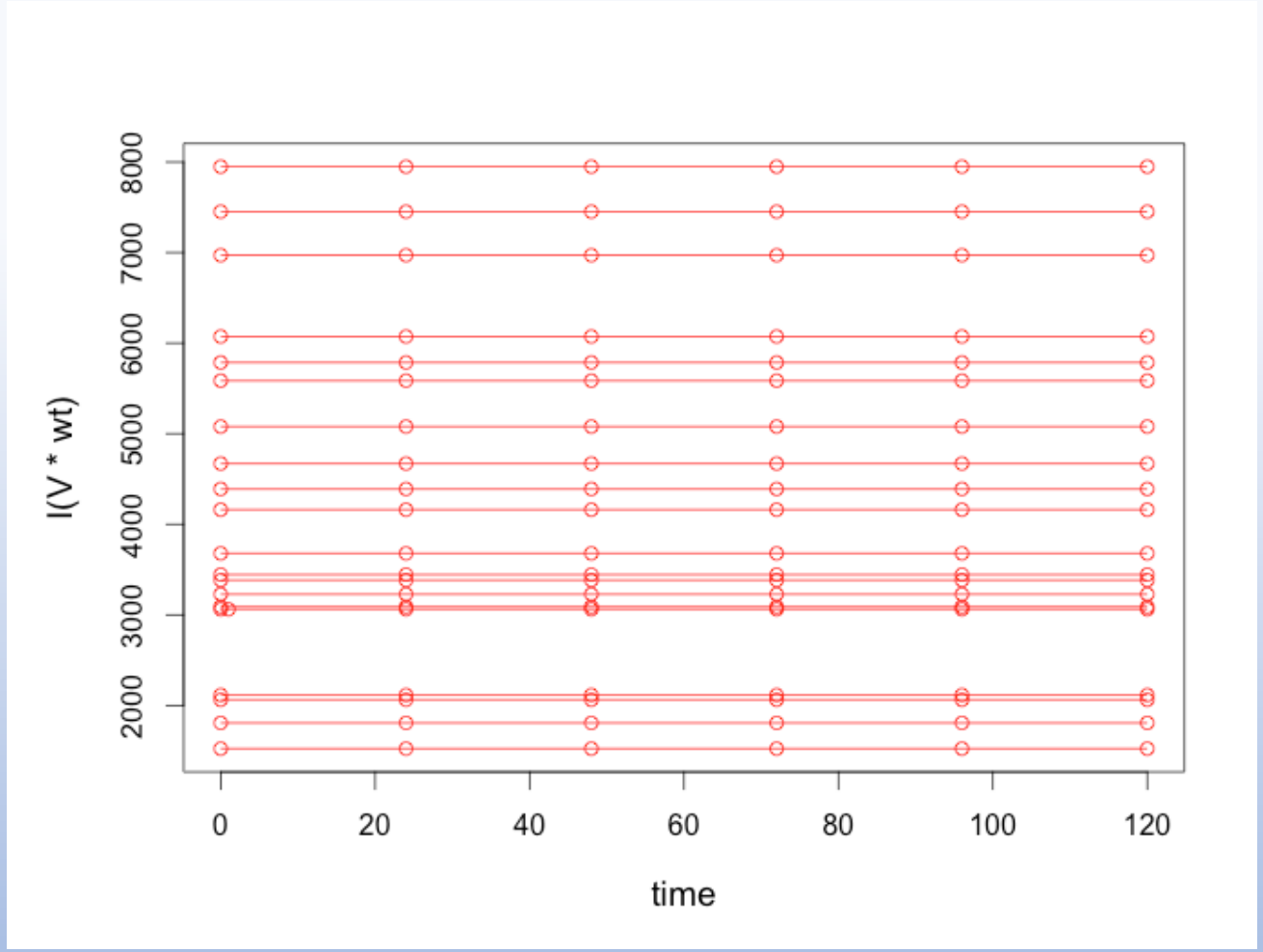
Plotting PMcov




```
run1$cov$plot(V~wt)
```




```
run1$cov$plot(Ke~age,lowess=F,reg=T,pch=3)
```




```
run1$cov$plot(I(V*wt)~time)
```

PMcov$step()

- Checks each parameter against all covariates in stepwise multivariate linear regression
- Model selection is by AIC
- Default is backwards selection, i.e. start with a parameter and all covariates, then successively remove parameters associated with the greatest AIC drop until no further improvement in AIC
- Report P-value of retained parameters in multivariate linear regression

PMstep

	Ka	Ke	V	Tlag1
wt	NA	NA	NA	0.1484646
africa	NA	NA	NA	NA
age	NA	NA	NA	NA
gender	NA	NA	NA	NA
height	NA	NA	NA	NA

```
run1$cov$step()
```

PMpop/post objects

- Predictions based on mean/median population or posterior Bayesian parameter values at `PM_fit$run(…, idelta)` frequency
- Only available after NPAG run
- class: PMpop/PMpost, data.frame
- methods: none (but can be plotted as argument to plot.PMmdata)
- examples: run1$post, run1$pop, run2$post, run2$pop.2

PMpop/post structure

- **id** Subject id
- **time** Time of predictions in decimal hours
- **icen** Prediction based on mean or median of Bayesian population/posterior parameter distribution
- **pred** Predicted output for each outeq
- **outeq** Output equation number
- **block** Observation blocks within subjects as defined by EVID=4 dosing events

PM_data objects

- The data file for the run
- class: PM_data
- methods: plot, summary
- examples: data1, data2

Summarizing PM_data

```
Number of subjects: 20
Number of inputs: 1
Number of outputs: 1
Total number of observations (outeq 1): 139, with 0 (0.000%) missing
Number of covariates: 5

THE FOLLOWING ARE MEAN (SD), MIN TO MAX
--------------------------------------------------------------------------------

INPUTS
Number of doses per subject (input 1): 6.000 (0.000), 6.000 to 6.000
Dose per subject (input 1): 585.000 (45.189), 450.000 to 600.000

OUTPUTS
Number of obs per subject (outeq 1): 6.950 (0.224), 6.000 to 7.000
Observation per subject (outeq 1): 7.241 (3.799), 1.860 to 20.150

COVARIATES
wt: 54.538 (7.173), 43.000 to 66.500
africa: 1.000 (0.000), 1.000 to 1.000
age: 27.035 (7.717), 19.000 to 54.000
gender: 0.749 (0.434), 0.000 to 1.000
height: 167.792 (7.562), 150.000 to 181.000
--------------------------------------------------------------------------------
Note: See help(summary.PMmatrix) for accessing specific items by name.
```

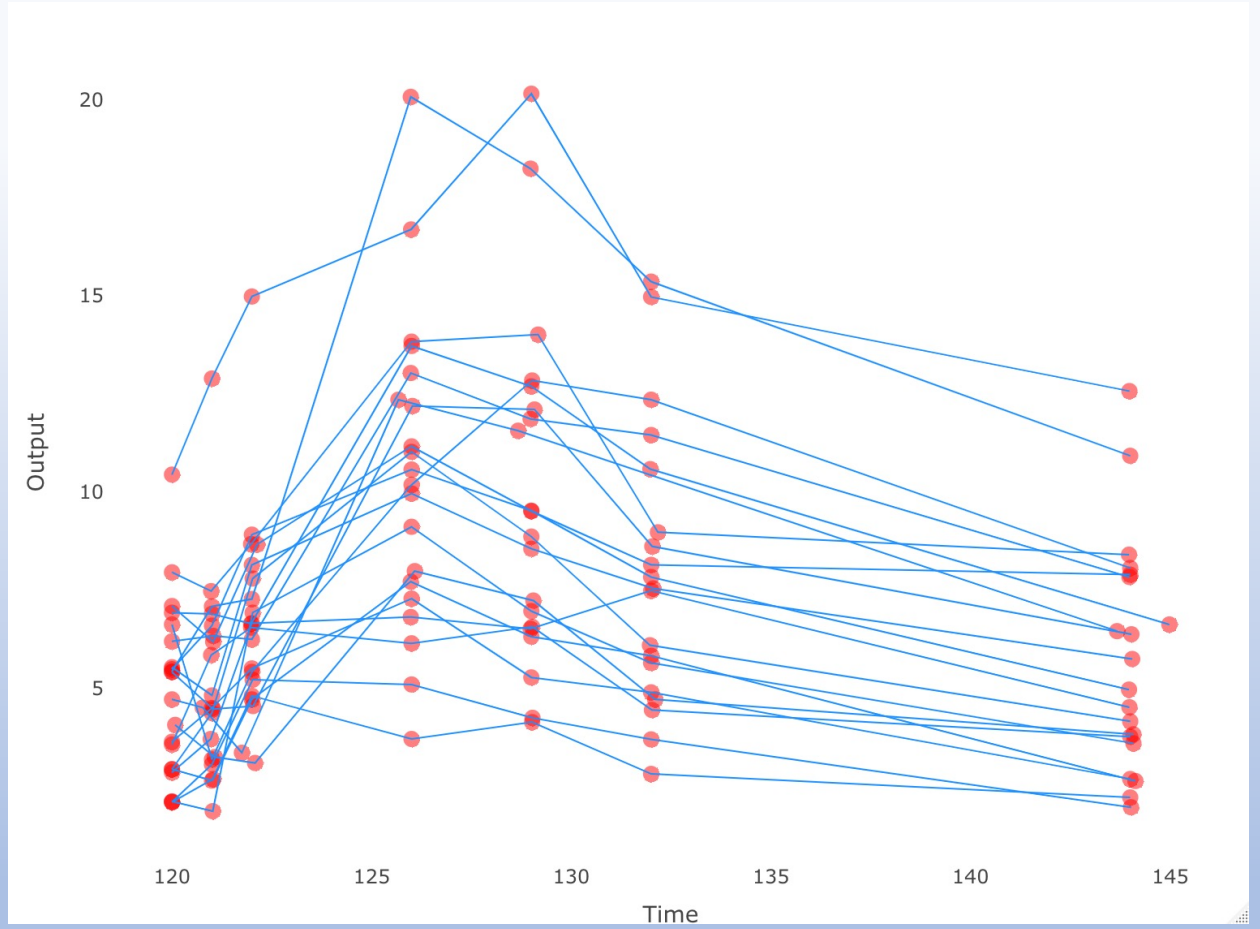
```
data1$summary()
```

Summarizing PM_data

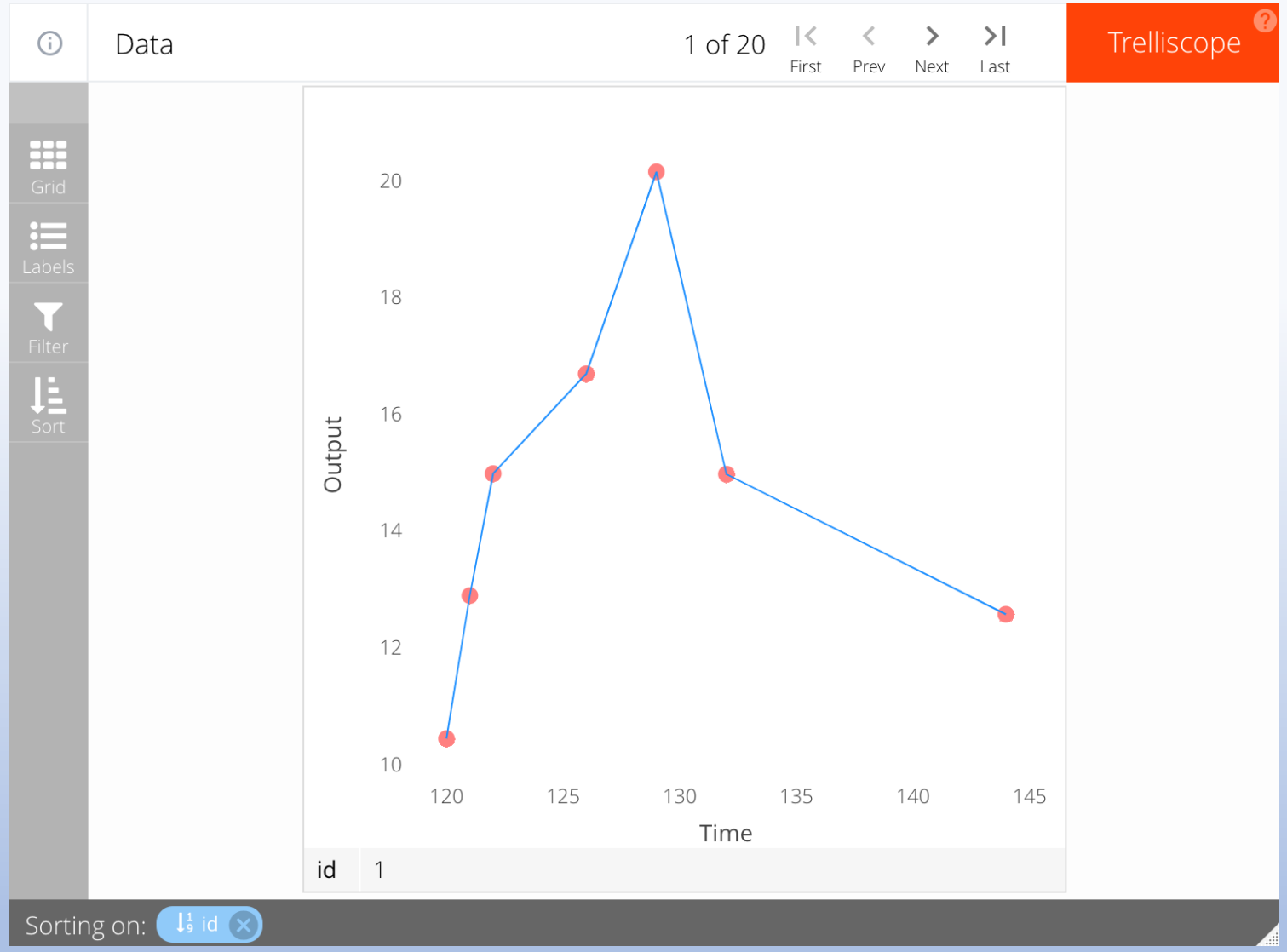
```
       id          I(dose/wt)
 Min.   : 1.00   Min.   : 9.023
 1st Qu.: 5.75   1st Qu.:10.081
 Median :10.50   Median :10.764
 Mean   :10.50   Mean   :10.844
 3rd Qu.:15.25   3rd Qu.:11.742
 Max.   :20.00   Max.   :12.848
```

```
dosekg <- data1$summary(formula = I(dose/wt)~id, FUN = mean)
summary(dosekg$formula)
```

Plotting PM_data




```
data1$plot()
```




```
data1$plot(overlay = F)
```

Getting help on plots

- `?PM_result`