EFSA-Project

Statistical Learning Theory

UNIPV
A.Y. 2020/2021
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- Domenico Ragusa

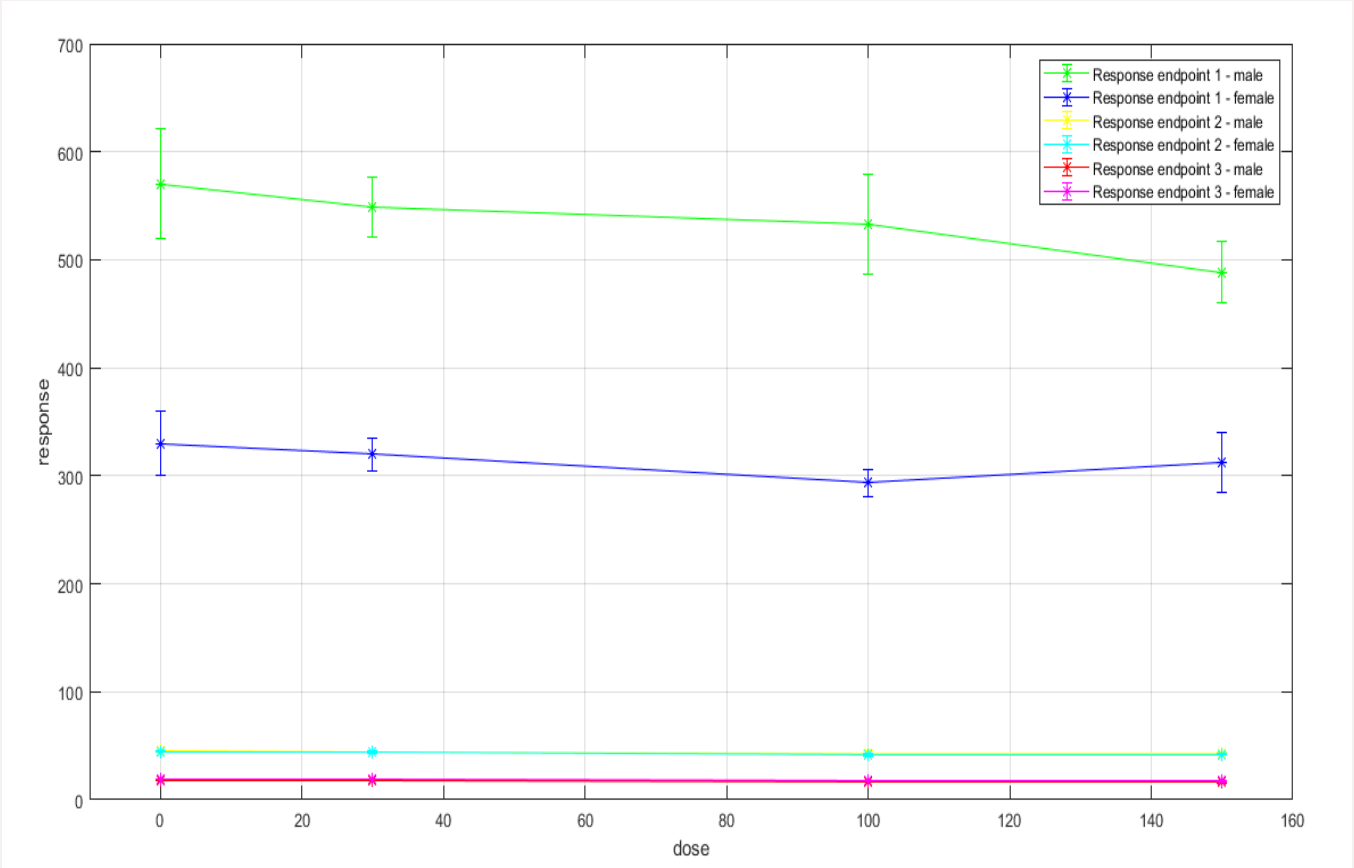
Goals

1. Plot dose-response data for each pair endpoint-gender (6 plots) with error bars reflecting error size on response measurements.
2. Use subset selection to estimate separate models for the 3 endpoints using gender as categorical variable.
3. Use subset selection to estimate a unique model using gender and endpoint as categorical variables.
4. In points 2. and 3., heteroscedasticity of the data should be taken into account.

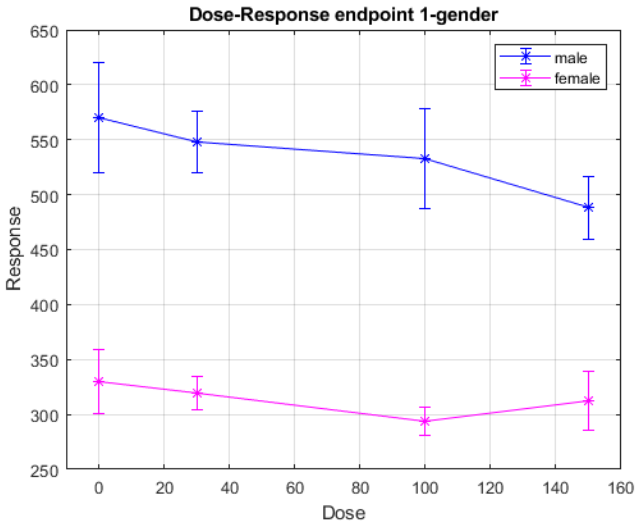
Data table

response	number of animals	SD	SE	variance	dose	sex (0=M, 1=F)	endpoint
570.4	9	75.6	25.200	635.040	0	0	1
548.5	10	44.3	14.009	196.249	30	0	1
533	10	72.3	22.863	522.729	100	0	1
488.1	9	42.5	14.167	200.694	150	0	1
329.8	10	46.8	14.799	219.024	0	1	1
319.7	10	24.3	7.684	59.049	30	1	1
293.3	10	20.1	6.356	40.401	100	1	1
312.4	10	43.1	13.629	185.761	150	1	1
45.2	9	1.5	0.500	0.250	0	0	2
44.6	10	1.7	0.538	0.289	30	0	2
43	10	3.8	1.202	1.444	100	0	2
42.8	9	1.7	0.567	0.321	150	0	2
44.7	10	1.3	0.411	0.169	0	1	2
44.1	10	1.6	0.506	0.256	30	1	2
41.5	10	1.6	0.506	0.256	100	1	2
42.1	10	1.2	0.379	0.144	150	1	2
18.3	9	0.5	0.167	0.028	0	0	3
17.9	10	0.5	0.158	0.025	30	0	3
16.5	10	0.6	0.190	0.036	100	0	3
16.3	9	0.8	0.267	0.071	150	0	3
19.1	10	0.5	0.158	0.025	0	1	3
19	10	0.4	0.126	0.016	30	1	3
17.9	10	0.5	0.158	0.025	100	1	3
17.3	10	0.6	0.190	0.036	150	1	3

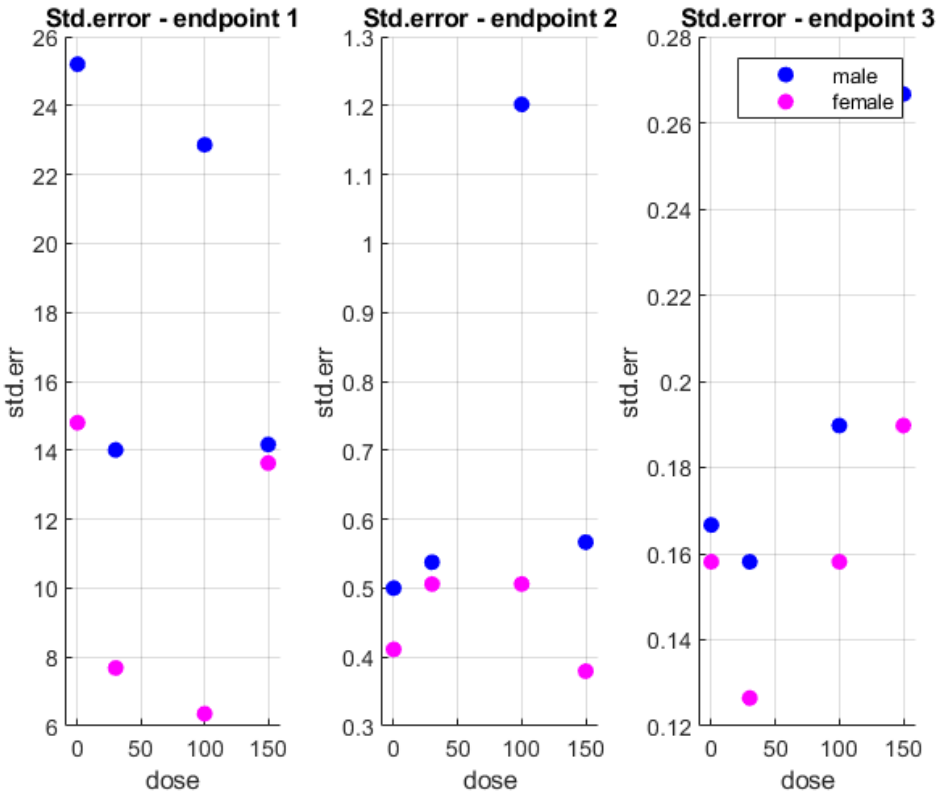
Data plot

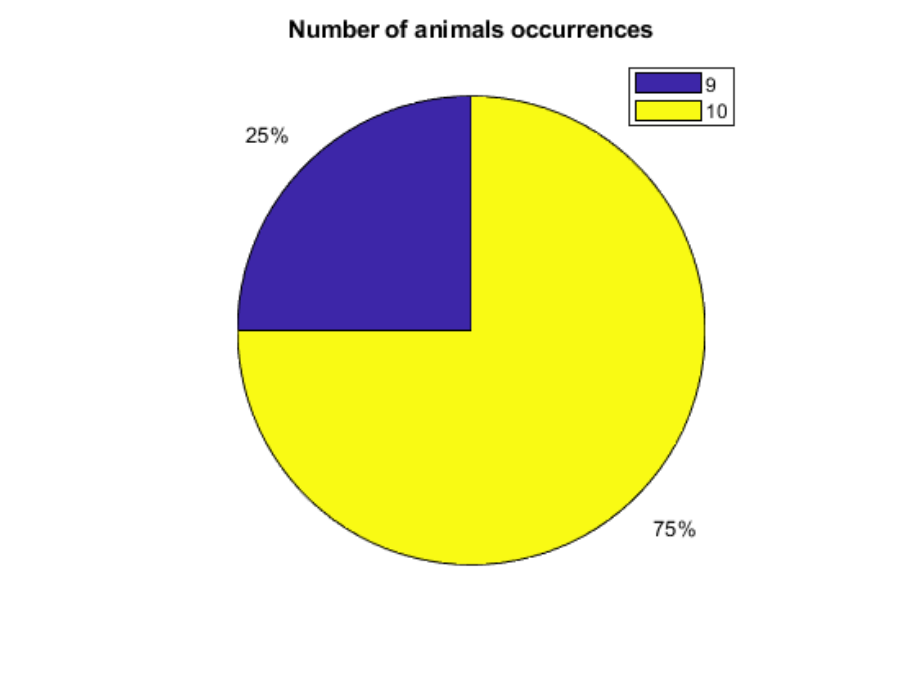

Response endpoint 1 - male
Response endpoint 1 - female
Response endpoint 2 - male
Response endpoint 2 - female
Response endpoint 3 - male
Response endpoint 3 - female
response
dose
0
100
200
300
400
500
600
700
0
20
40
60
80
100
120
140
160

Dose - response data plot



Looking at the data in advance





How to work

Alternatives:

- Linear models -> 👍
- Fourier series -> No period, few data
- Polynomial models -> few data (not beyond 2° degree)

Approaches:

- Forward stepwise selection
- Backward stepwise selection
- Forward-Backward stepwise selection (stepwiselm)

Take into account heteroscedasticity:

$$w_{ii} = \frac{1}{std.error^2}, \qquad std.error^2 = \frac{\sigma_i^2}{n}$$

Forward stepwise selection

1. M_0: null model (no predictors).

2. For k = 0, . . . ,p − 1:
    2.1 Consider all p − k models with one additional predictor.
    2.2 Choose the best, call it Mk+1.
        Best: smallest RSS or highest R2.

3. Select the best model using objective tests.

Backward Stepwise Selection

1. *Mp*: full model (all p predictors).
2. For k = p, p-1,..., 1:
    - 2.1 Consider all k.
    - 2.2 Choose the best among these k models and call it *Mk1*. (smallest RSS or highest R^2).
3. Select the best model using objective tests.

Function: stepwiselm

stepwiselm

Perform stepwise regression

co

Syntax

```
mdl = stepwiselm(tbl)
mdl = stepwiselm(X,y)
mdl = stepwiselm( __ ,modelspec)
mdl = stepwiselm( __ ,Name,Value)
```

Description

`mdl = stepwiselm(tbl)` creates a linear model for the variables in the table or dataset array `tbl` using stepwise regression to add or remove predictors, starting from a constant model. `stepwiselm` uses the last variable of `tbl` as the response variable. `stepwiselm` uses forward and backward stepwise regression to determine a final model. At each step, the function searches for terms to add the model to or remove from the model, based on the value of the `'Criterion'` argument.

`mdl = stepwiselm(X,y)` creates a linear model of the responses `y` to the predictor variables in the data matrix `X`.

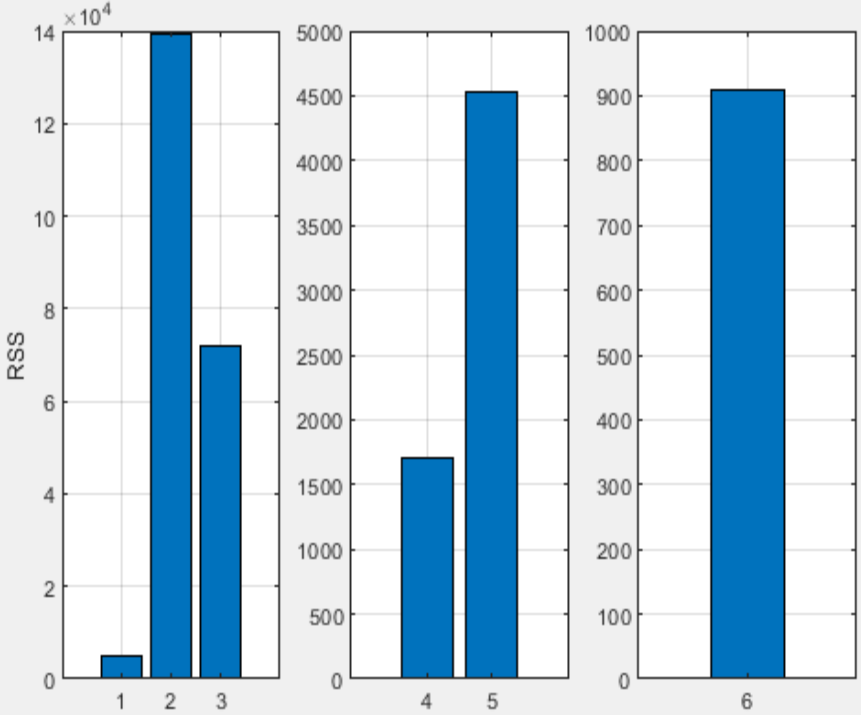
`mdl = stepwiselm( __ ,modelspec)` specifies the starting model `modelspec` using any of the input argument combinations in previous syntaxes.

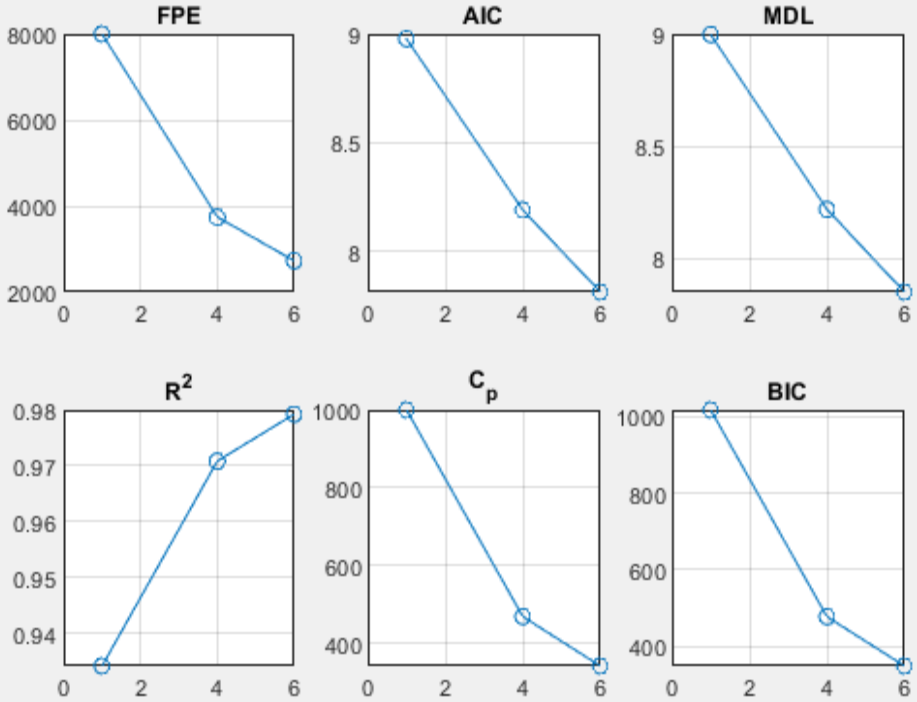
`mdl = stepwiselm( __ ,Name,Value)` specifies additional options using one or more name-value pair arguments. For example, you can specify the categorical variables, the smallest or largest set of terms to use in the model, the maximum number of steps to take, or the criterion that `stepwiselm` uses to add or remove terms.

http://it.mathworks.com/help/stats/stepwiselm.html

Forward (Backward) Selection – endpoint 1

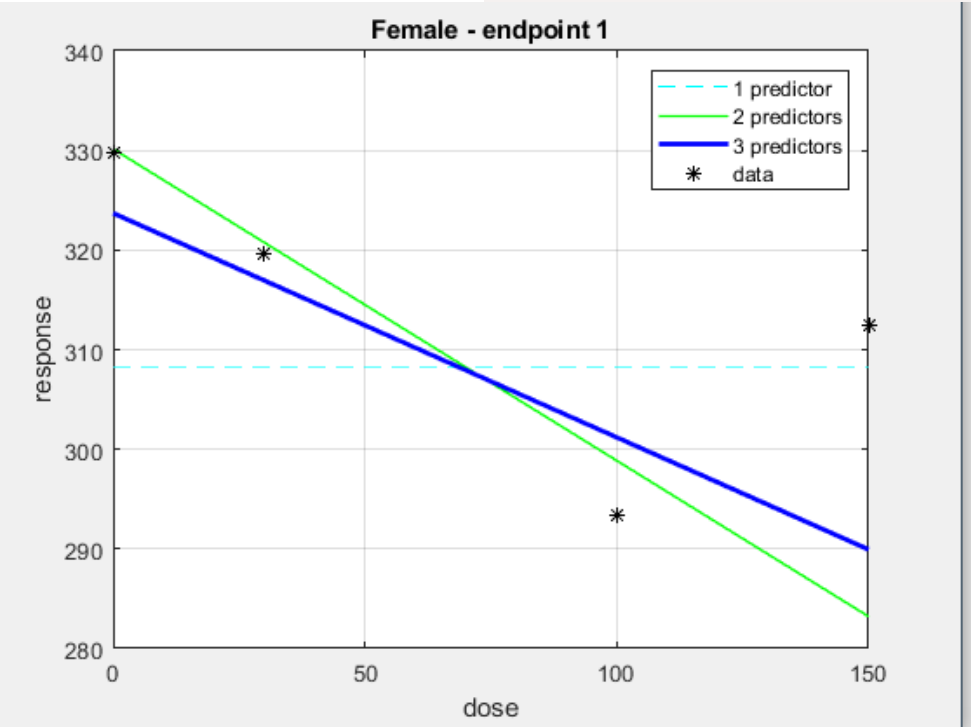
$$response = 567.3801 - 243.6787 * sex - 0.5059 * dose + 0.2808 * sex * dose$$

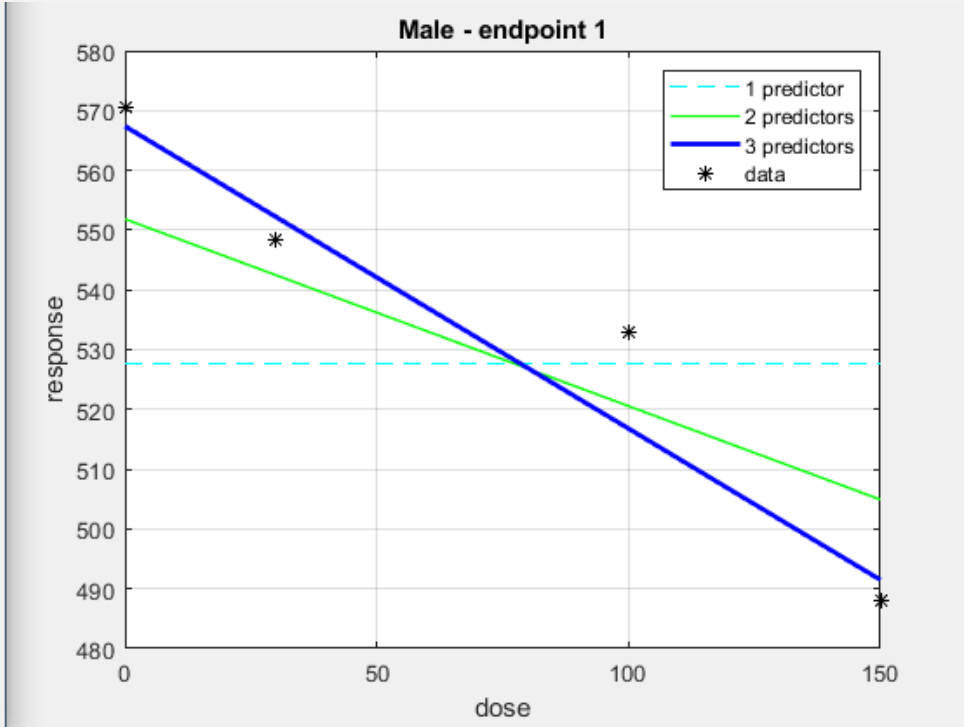




Forward (Backward) Selection – endpoint 1

theta	std.error
567.3801	16.4684625
-243.679	19.0457353
-0.50592	0.16458333
0.280831	0.19849252





StepwiseLM (forward-backward) – endpoint 1

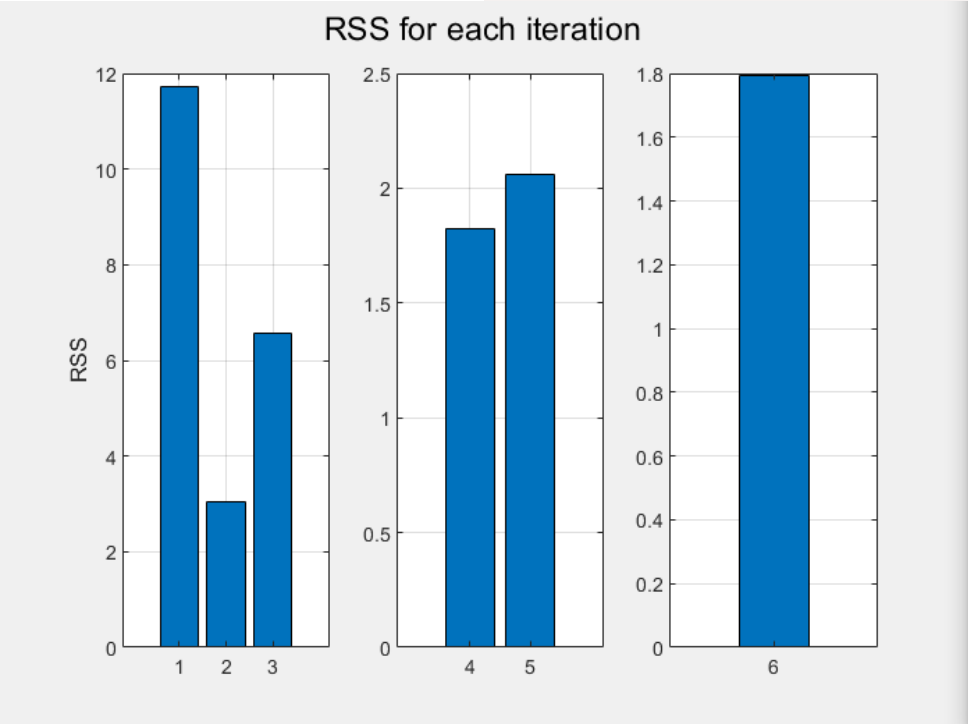
```
mdl_1 =
Linear regression model:
    response_1 ~ 1 + dose_1 + gender_female_1

Estimated Coefficients:
                          Estimate       SE        tStat       pValue
                          ________    ______    _______    _________

    (Intercept)             551.84    13.447     41.039    1.6201e-07
    dose_1                 -0.31284    0.1008    -3.1037      0.026742
    gender_female_1_1        -221.7    12.073    -18.363    8.8074e-06


Number of observations: 8, Error degrees of freedom: 5
Root Mean Squared Error: 1.25
R-squared: 0.986,  Adjusted R-Squared: 0.98
F-statistic vs. constant model: 171, p-value = 2.5e-05
```

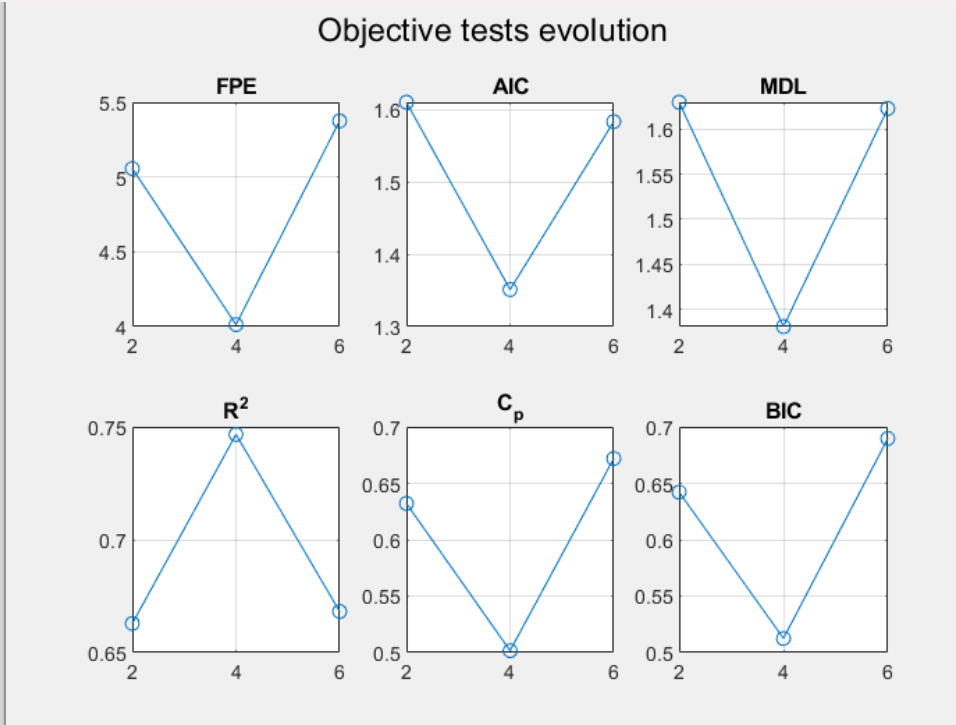
Confidence intervals

517.2787	586.4103
-0.5720	-0.0537
-252.7355	-190.6660

Forward (Backward) Selection – endpoint 2

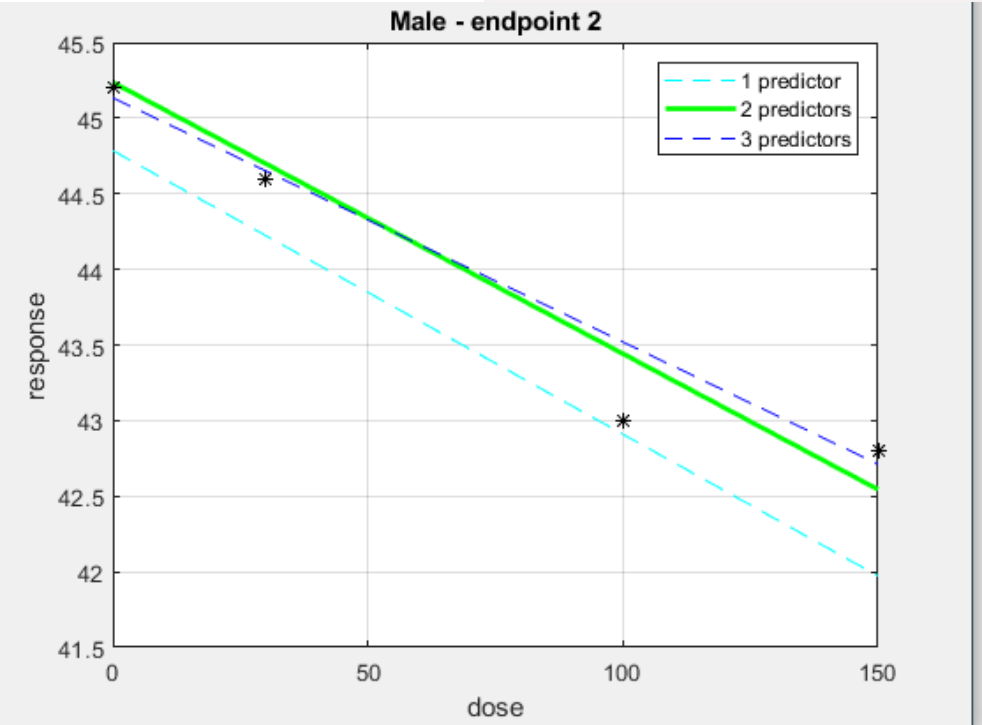
$$response = 45.2371 - 0.0180 * sex - 0.7831 * dose$$

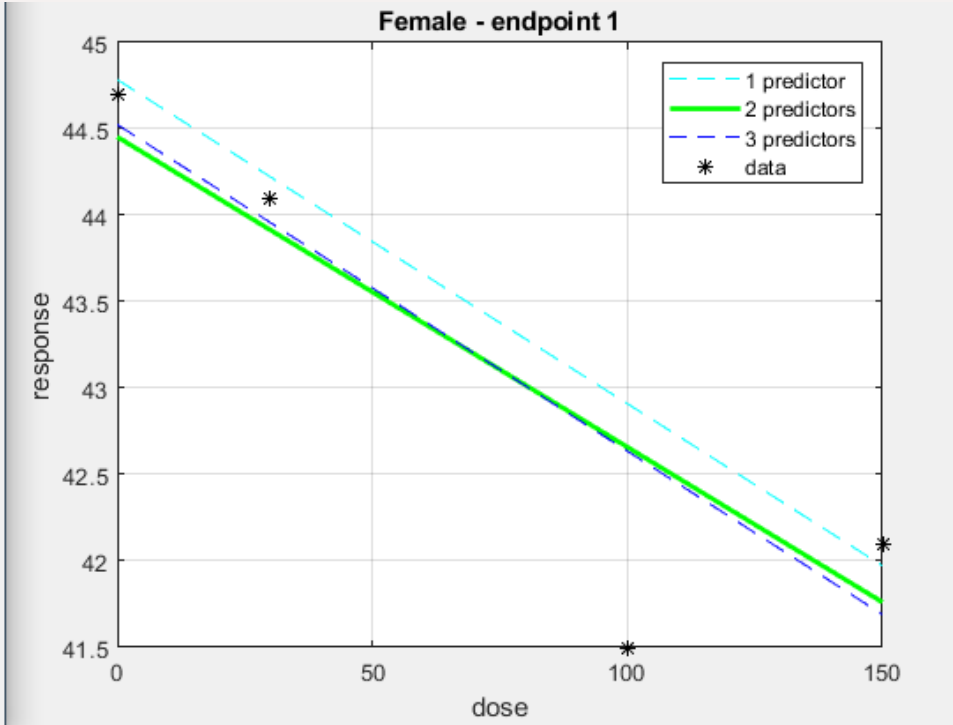




Forward (Backward) Selection – endpoint 2

theta	std.error
45.23707	0.39747548
-0.01795	0.00330656
-0.78308	0.43948087





StepwiseLM (forward-backward) – endpoint 2

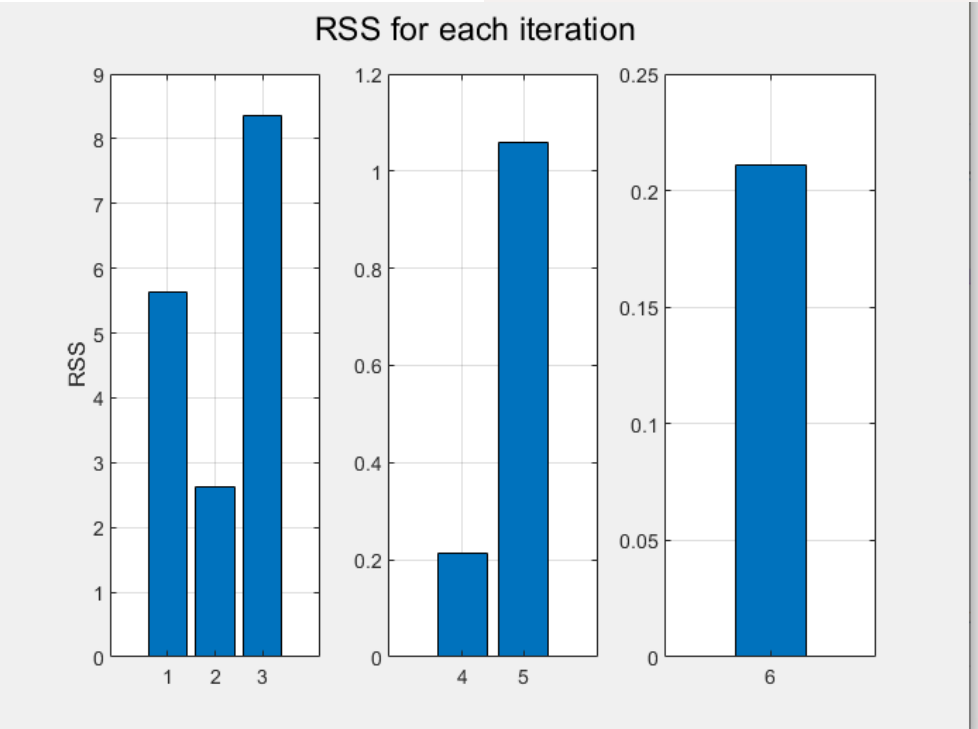
```
mdl_2 =
Linear regression model:
    response_2 ~ 1 + dose_2

Estimated Coefficients:
                   Estimate        SE         tStat       pValue
                   ________    ________    _______    __________

    (Intercept)       44.785     0.35731     125.34    1.7391e-11
    dose_2         -0.018754   0.0038235    -4.9048     0.0026978


Number of observations: 8, Error degrees of freedom: 6
Root Mean Squared Error: 1.37
R-squared: 0.8,  Adjusted R-Squared: 0.767
F-statistic vs. constant model: 24.1, p-value = 0.0027
```

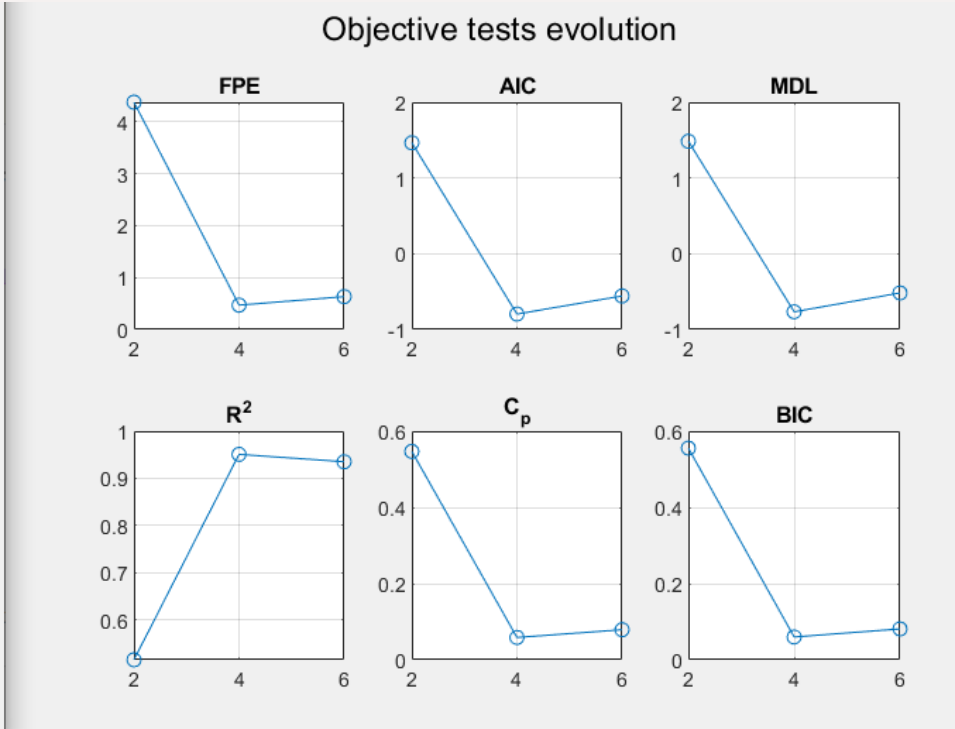
Confidence intervals

43.991	45.6596
-0.0281	-0.0094

Forward (Backward) Selection – endpoint 3

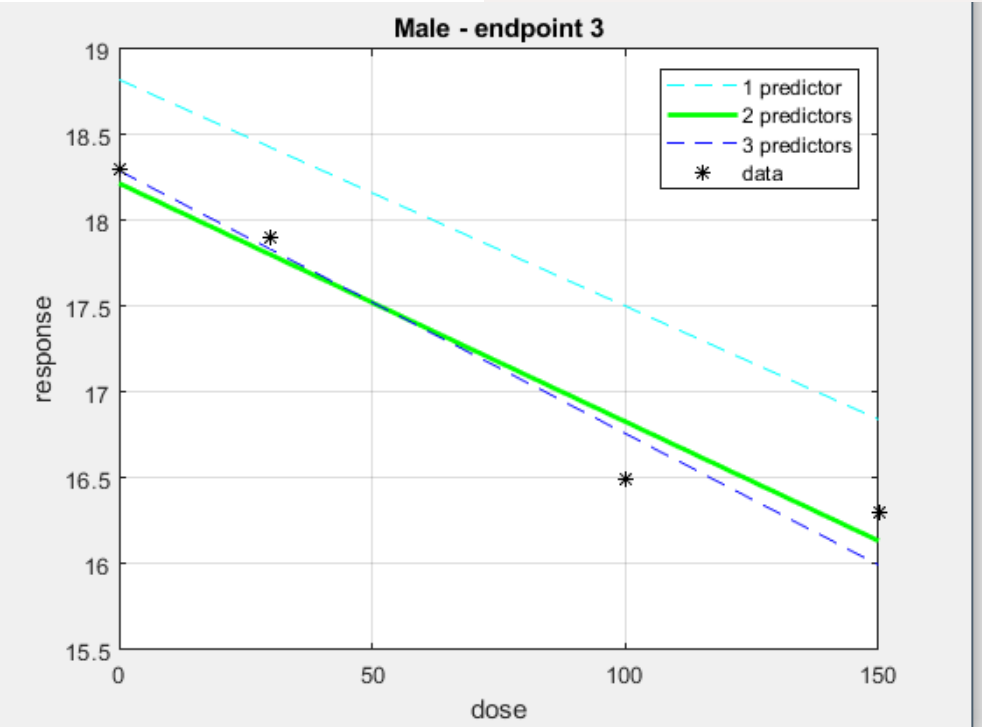
$$response = 18.2186 - 0.0139 * sex + 1.0881 * dose$$

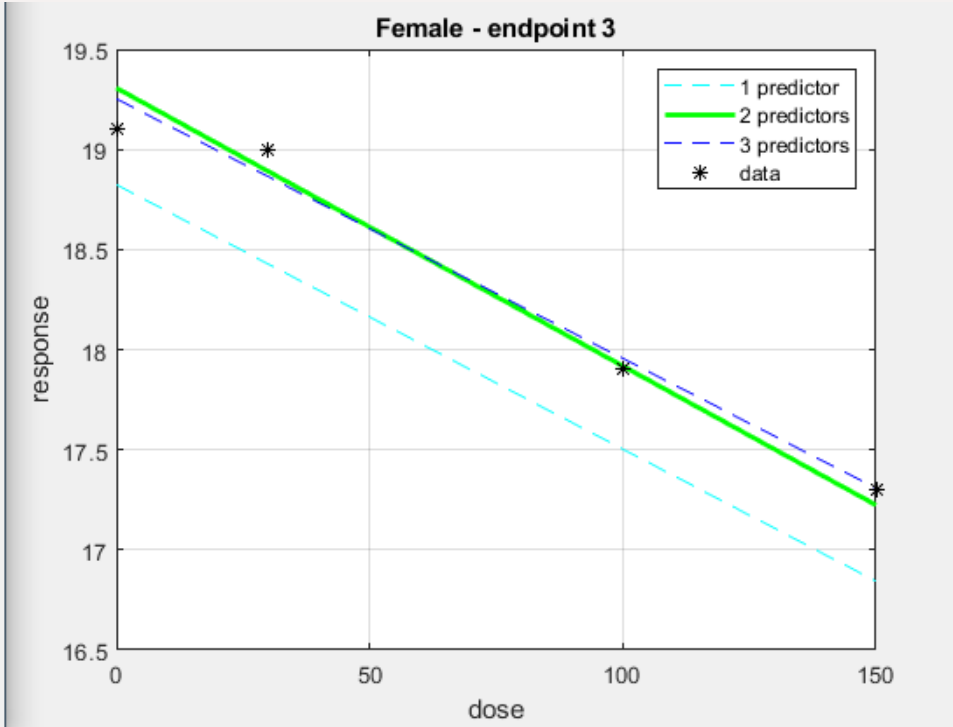




Forward (Backward) Selection – endpoint 3

theta	std.error
18.21858	0.1254263
-0.01389	0.00128698
1.088115	0.13866997





StepwiseLM (forward-backward) – endpoint 3

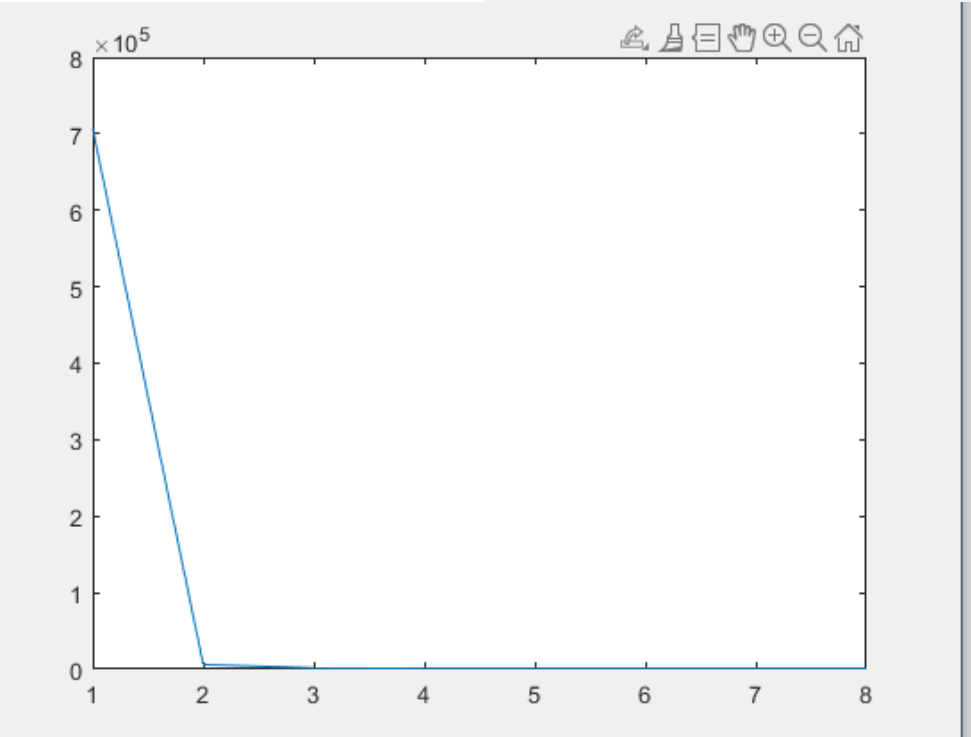
```
mdl_3 =
Linear regression model:
    response_3 ~ 1 + dose_3 + gender_female_3

Estimated Coefficients:
                          Estimate        SE        tStat       pValue
                          ________    ________    ______    __________

    (Intercept)              18.219     0.12543    145.25     2.934e-10
    dose_3                -0.013887    0.001287    -10.79    0.00011858
    gender_female_3_1        1.0881     0.13867    7.8468    0.00053962


Number of observations: 8, Error degrees of freedom: 5
Root Mean Squared Error: 1.15
R-squared: 0.971,  Adjusted R-Squared: 0.959
F-statistic vs. constant model: 83.6, p-value = 0.000144
```

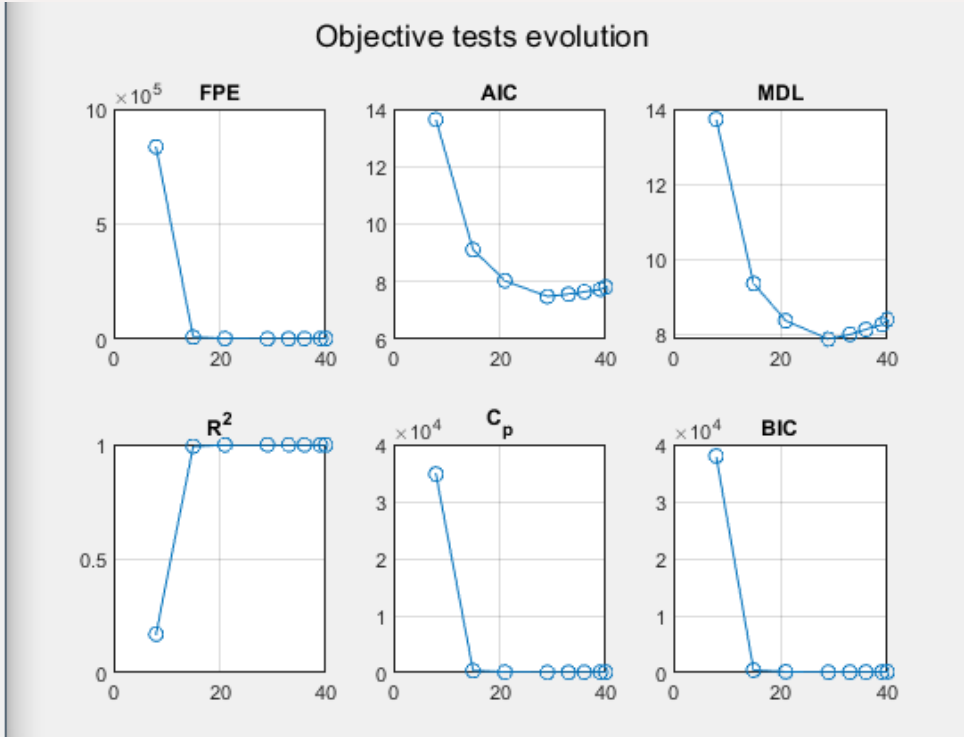
Confidence intervals

17.8962	18.5410
-0.0172	-0.0106
0.7317	1.4446

Forward selection – unique model

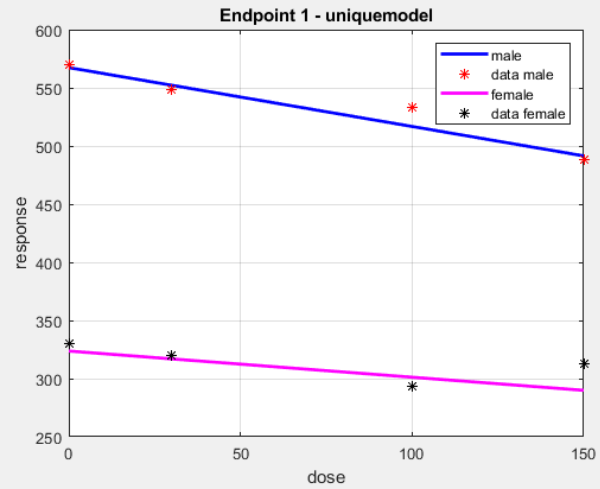
$$response = 18.36327 + 0.909607 * sex - 0.01459 * dose + 549.0169 * endpoint1 + 25.54763 * endpoint2 - 0.49133 * dose * endpoint1 - 244.588 * sex * endpoint1 + 0.280831 * sex * endpoint1 * dose$$

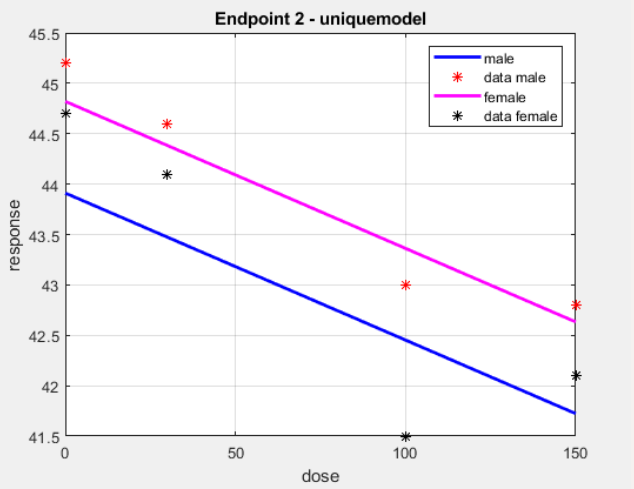


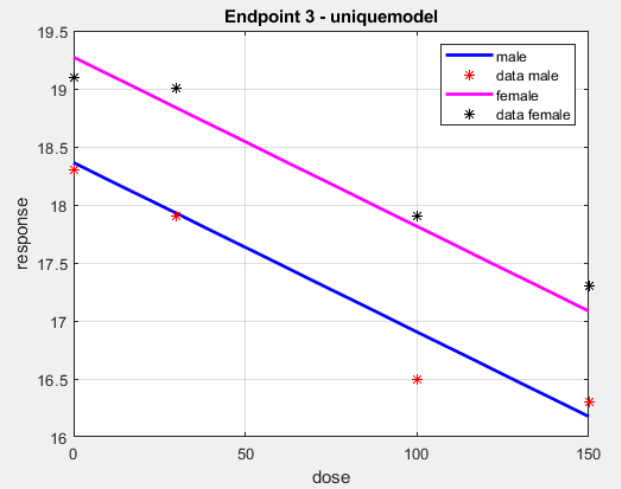


Forward (Backward) selection – unique model

Theta	Std. Error
18.36327	0.1750687
0.909607	0.1925467
-0.01459	0.0017444
549.0169	24.3243
25.54763	0.3149547
-0.49133	0.2430934
-244.588	28.130922
0.280831	0.2931705







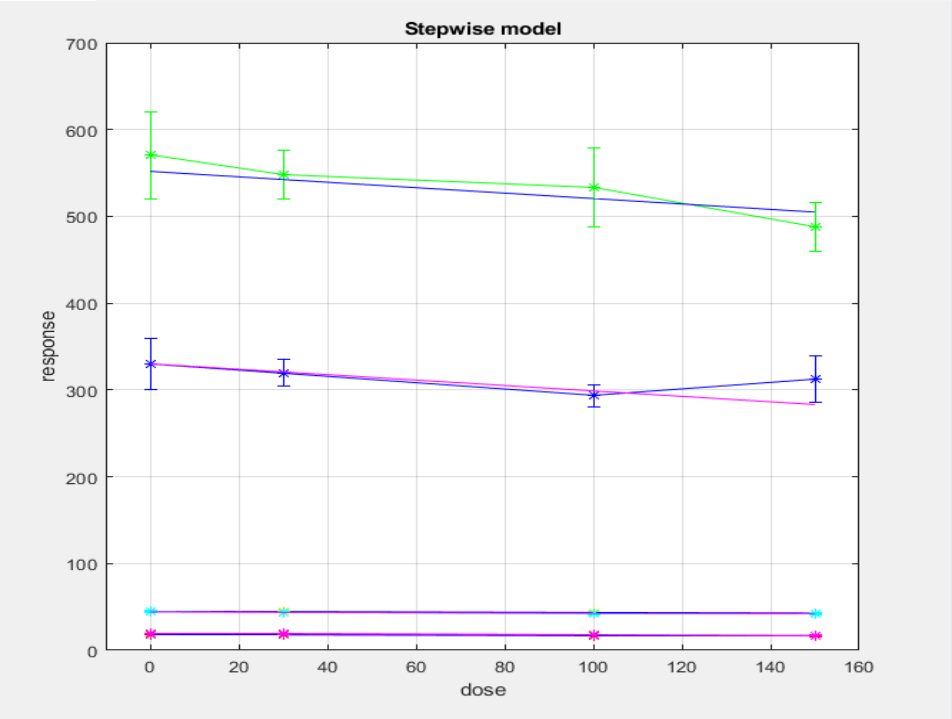
StepwiseLM (forward-backward) – unique model

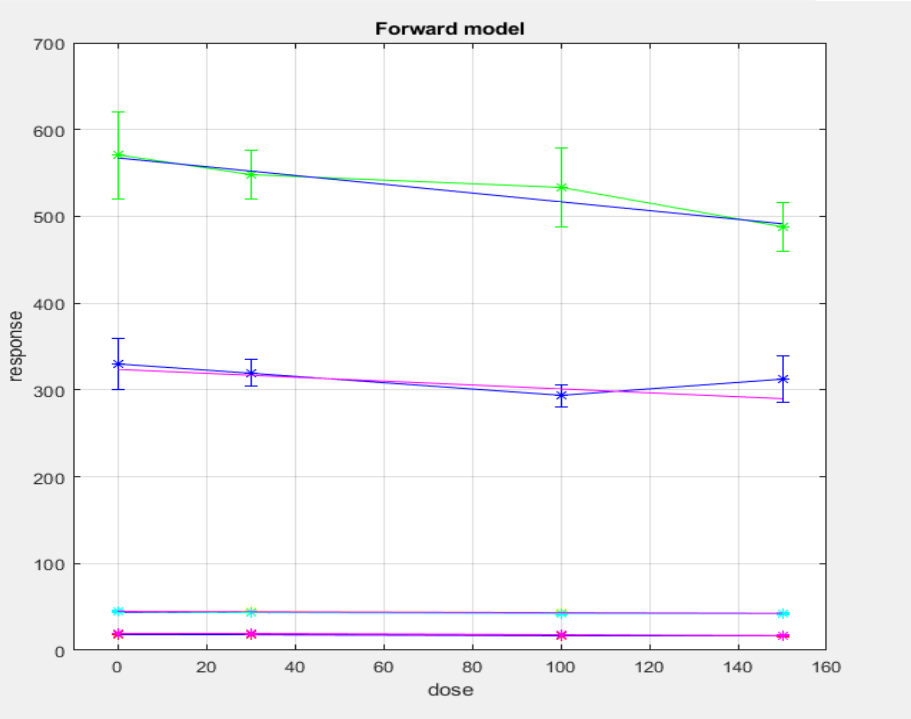
Confidence intervals

17.9752	18.5190
-0.0171	-0.0118
0.7858	1.3985
506.1281	561.0667
25.9946	27.5863
-0.5043	-0.0925
-247.4567	-198.1291
-2.9325	-0.9453

```
mdl =
Linear regression model:
    response ~ 1 + dose*endpoint_1 + female*endpoint_1 + female*endpoint_2

Estimated Coefficients:
                              Estimate        SE         tStat       pValue
                              ________    ________    _______    __________

    (Intercept)                 18.247     0.12825     142.28    2.9732e-26
    dose                     -0.014438   0.0012474    -11.575    3.4626e-09
    female_1                    1.0922     0.14453     7.5566    1.1526e-06
    endpoint_1_1                 533.6      12.958      41.18     1.149e-17
    endpoint_2_1                 26.79     0.37542     71.361    1.8213e-21
    dose:endpoint_1_1         -0.29841    0.097136     -3.072     0.0072948
    female_1:endpoint_1_1      -222.79      11.634     -19.149    1.8681e-12
    female_1:endpoint_2_1      -1.9389      0.4687     -4.1368    0.00077449


Number of observations: 24, Error degrees of freedom: 16
Root Mean Squared Error: 1.2
R-squared: 0.999,  Adjusted R-Squared: 0.999
F-statistic vs. constant model: 2.62e+03, p-value = 2.96e-23
```

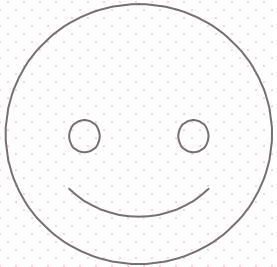
Jump to the conclusions





Response endpoint 1 - male
Predicted response endpoint 1 - male
Response endpoint 1 - female
Predicted response endpoint 1 - female
Response endpoint 2 - male
Predicted response endpoint 2 - male
Response endpoint 2 - female
Predicted response endpoint 2 - female
Response endpoint 3 - male
Predicted response endpoint 3 - male
Response endpoint 3 - female
Predicted response endpoint 3 - female

Grazie per l’attenzione



Repository: https://github.com/domenico-rgs/EFSA-Project