STA721 Final Project

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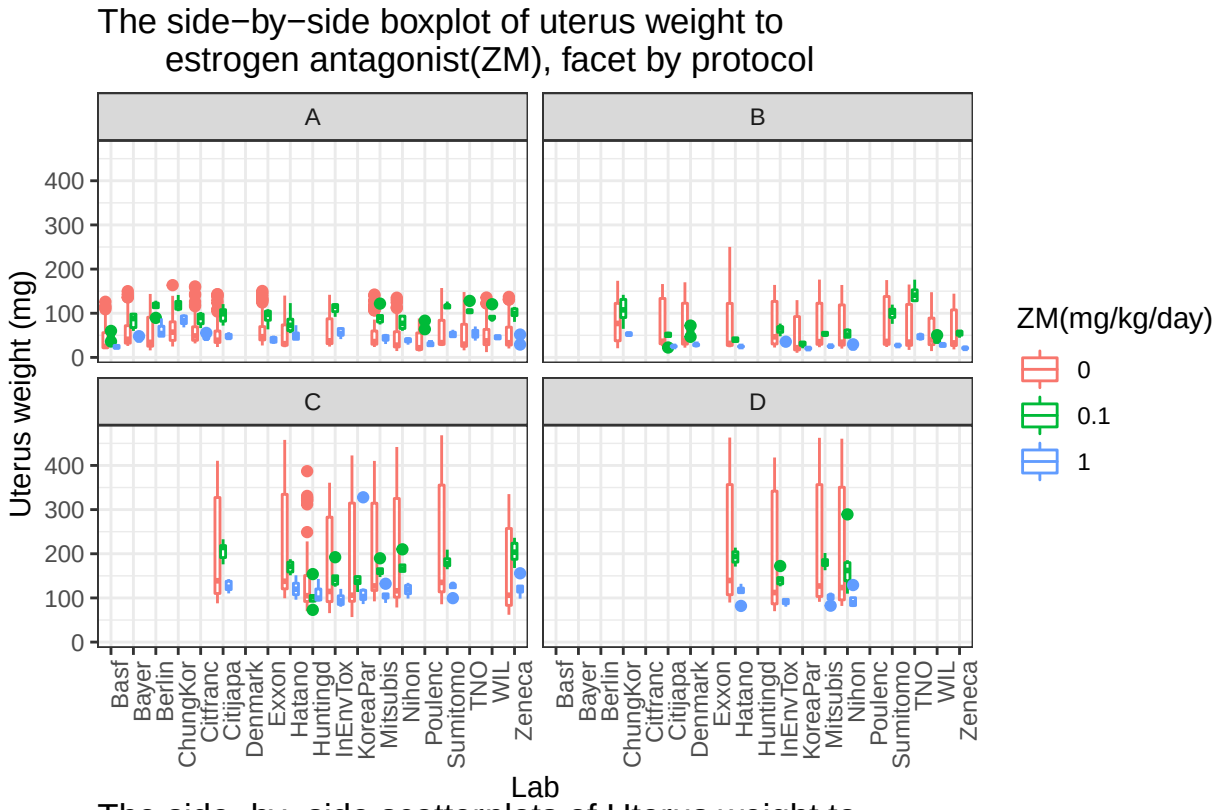
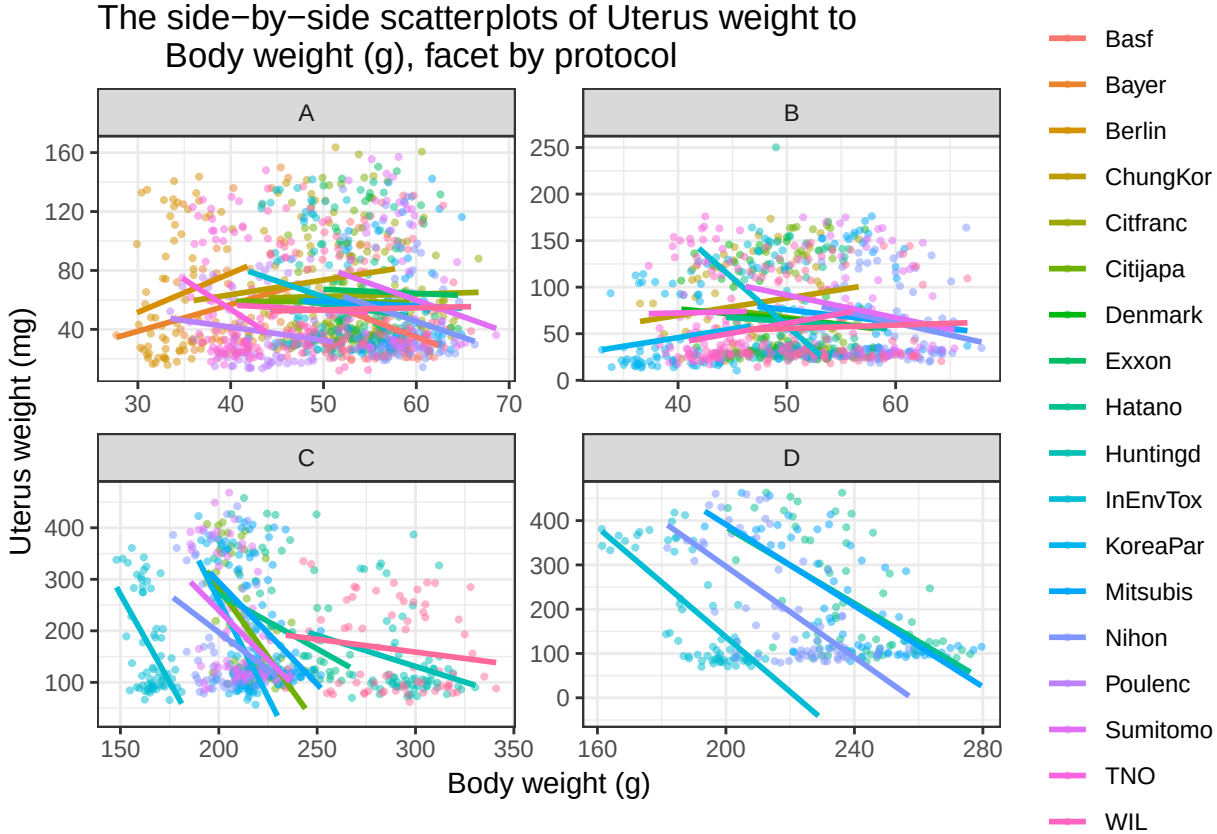
4. Conclusion


The side−by−side boxplot of uterus weight to
estrogen antagonist(ZM), facet by protocol
A
B
C
D
Uterus weight (mg)
0
100
200
300
400
Basf
Bayer
Berlin
ChungKor
Citfranc
Citijapa
Denmark
Exxon
Hatano
Huntingd
InEnvTox
KoreaPar
Mitsubis
Nihon
Poulenc
Sumitomo
TNO
WIL
Zeneca
Lab
ZM(mg/kg/day)
0
0.1
1


The side−by−side scatterplots of Uterus weight to
Body weight (g), facet by protocol
A
B
C
D
Uterus weight (mg)
Body weight (g)
Basf
Bayer
Berlin
ChungKor
Citfranc
Citijapa
Denmark
Exxon
Hatano
Huntingd
InEnvTox
KoreaPar
Mitsubis
Nihon
Poulenc
Sumitomo
TNO
WIL

Apeendix

EDA

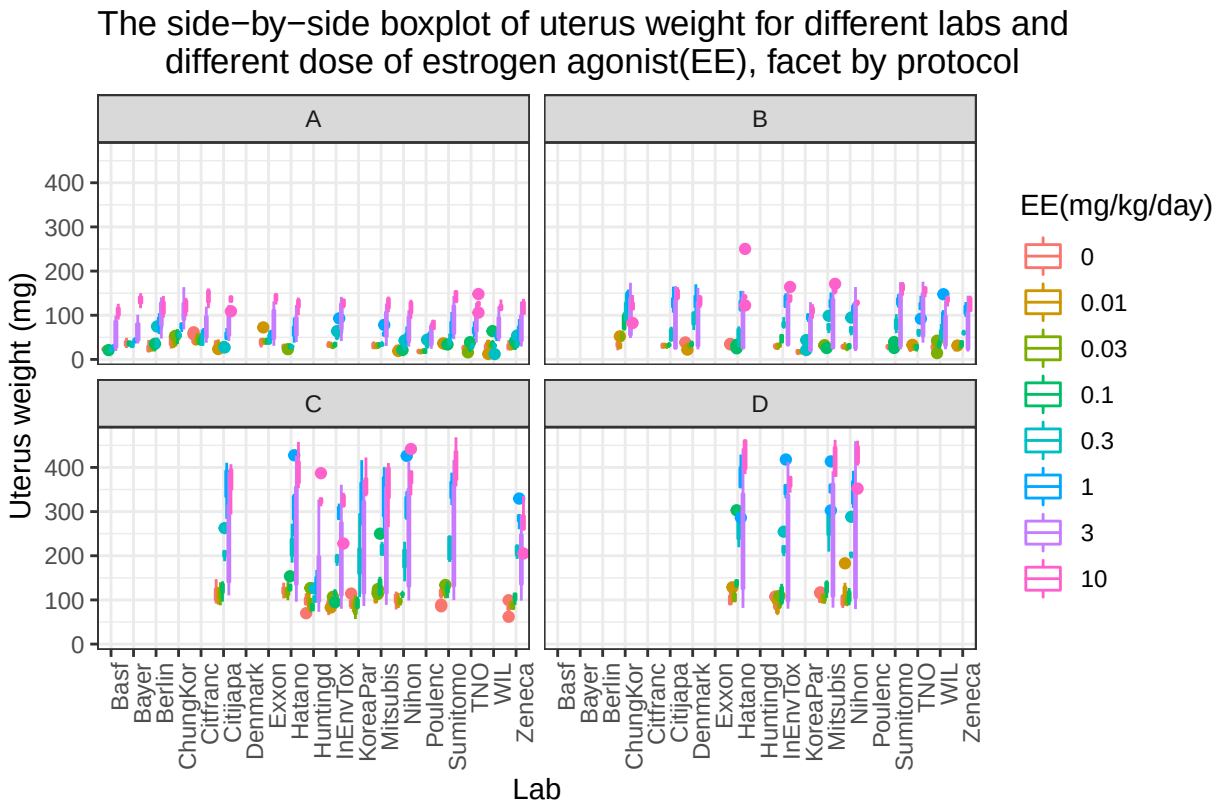
```
bioassay_lm = bioassay[,-7]
str(bioassay_lm)
```

```
## 'data.frame':    2677 obs. of  6 variables:
##  $ uterus  : num  21 22 21 26 24 25 22 26 24 22 ...
##  $ weight  : num  61.9 55.9 59.1 54.8 57.5 57.6 60.3 59 59.1 61.4 ...
##  $ protocol: Factor w/ 4 levels "A","B","C","D": 1 1 1 1 1 1 1 1 1 1 ...
##  $ EE      : Factor w/ 8 levels "0","0.01","0.03",..: 1 1 1 1 1 1 1 1 1 1 ...
##  $ ZM      : Factor w/ 3 levels "0","0.1","1": 1 1 1 1 1 1 1 1 1 1 ...
##  $ lab     : Factor w/ 19 levels "Basf","Bayer",..: 1 1 1 1 1 1 1 1 1 1 ...
```

```
table(bioassay_lm$EE, bioassay_lm$ZM)
```

```
##
##           0 0.1   1
##   0    484   0   0
##   0.01 234   0   0
##   0.03 239   0   0
##   0.1  246   0   0
##   0.3  246   0   0
##   1    246   0   0
##   3    246 245 246
##   10   245   0   0
```

```
ggplot(data=bioassay,mapping = aes(y = uterus,x = lab,color=EE))+
  geom_boxplot()+theme_bw()+facet_wrap(~ protocol) +
  theme(axis.text.x = element_text(angle = 90, hjust = 1)) +
  labs(x = "Lab", y="Uterus weight (mg)", title="The side-by-side boxplot of uterus weight for differen
       different dose of estrogen agonist(EE), facet by protocol", caption="", colour="EE(mg/kg/day)")
```



Model Part I

```
lm1 = lm(uterus~., data = bioassay_lm)
summary(lm1)
```

```
##
## Call:
## lm(formula = uterus ~ ., data = bioassay_lm)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -107.625  -30.150    2.595   21.979  190.872
##
## Coefficients:
##               Estimate Std. Error t value Pr(>|t|)
## (Intercept)   15.82251    6.55993   2.412 0.015933 *
## weight        -0.45365    0.05508  -8.237 2.75e-16 ***
## protocolB      7.84315    2.26416   3.464 0.000541 ***
## protocolC    207.53588    9.48173  21.888  < 2e-16 ***
## protocolD    221.22623   10.07610  21.956  < 2e-16 ***
## EE0.01        -0.60177    3.31535  -0.182 0.855982
## EE0.03         0.26008    3.28953   0.079 0.936989
## EE0.1          8.01257    3.25677   2.460 0.013946 *
## EE0.3         47.94479    3.25716  14.720  < 2e-16 ***
## EE1          106.35605    3.26542  32.570  < 2e-16 ***
## EE3          136.45891    3.27333  41.688  < 2e-16 ***
## EE10         150.55730    3.28955  45.768  < 2e-16 ***
```

```
## ZM0.1        -80.51563    3.75770 -21.427  < 2e-16 ***
## ZM1         -127.18576    3.75162 -33.902  < 2e-16 ***
## labBayer       2.60266    7.88343   0.330 0.741318
## labBerlin     14.84134    7.55929   1.963 0.049713 *
## labChungKor   32.46041    6.63073   4.895 1.04e-06 ***
## labCitfranc   26.21060    7.45111   3.518 0.000443 ***
## labCitijapa   21.52689    6.33273   3.399 0.000686 ***
## labDenmark    18.95727    7.80137   2.430 0.015165 *
## labExxon      23.72114    7.62673   3.110 0.001889 **
## labHatano     26.83352    6.19974   4.328 1.56e-05 ***
## labHuntingd    0.09856    8.84741   0.011 0.991112
## labInEnvTox    0.58445    6.38094   0.092 0.927028
## labKoreaPar   -2.51500    6.88744  -0.365 0.715023
## labMitsubis   24.63683    6.19749   3.975 7.22e-05 ***
## labNihon      13.18893    6.20345   2.126 0.033590 *
## labPoulenc    -4.14169    7.49225  -0.553 0.580450
## labSumitomo   28.52520    6.32781   4.508 6.83e-06 ***
## labTNO        16.56429    6.68045   2.480 0.013218 *
## labWIL        10.05022    6.63237   1.515 0.129809
## labZeneca     17.93047    6.42998   2.789 0.005332 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 41.56 on 2645 degrees of freedom
## Multiple R-squared:  0.802,  Adjusted R-squared:  0.7997
## F-statistic: 345.7 on 31 and 2645 DF,  p-value: < 2.2e-16
```

```
step(lm1, k=log(2677))
```

```
## Start:  AIC=20175.57
## uterus ~ weight + protocol + EE + ZM + lab
##
##            Df Sum of Sq      RSS   AIC
## <none>                   4568714 20176
## - lab      18    304839  4873553 20206
## - weight    1    117187  4685901 20236
## - protocol  3    855660  5424374 20612
## - ZM        2   2030817  6599531 21144
## - EE        7   7683826 12252540 22761
```

```
##
## Call:
## lm(formula = uterus ~ weight + protocol + EE + ZM + lab, data = bioassay_lm)
##
## Coefficients:
## (Intercept)       weight    protocolB    protocolC    protocolD
##    15.82251     -0.45365      7.84315    207.53588    221.22623
##      EE0.01       EE0.03        EE0.1        EE0.3          EE1
##    -0.60177      0.26008      8.01257     47.94479    106.35605
##         EE3          EE10        ZM0.1          ZM1     labBayer
##   136.45891    150.55730    -80.51563   -127.18576      2.60266
##   labBerlin  labChungKor  labCitfranc  labCitijapa   labDenmark
##    14.84134     32.46041     26.21060     21.52689     18.95727
##    labExxon    labHatano  labHuntingd  labInEnvTox  labKoreaPar
##    23.72114     26.83352      0.09856      0.58445     -2.51500
```

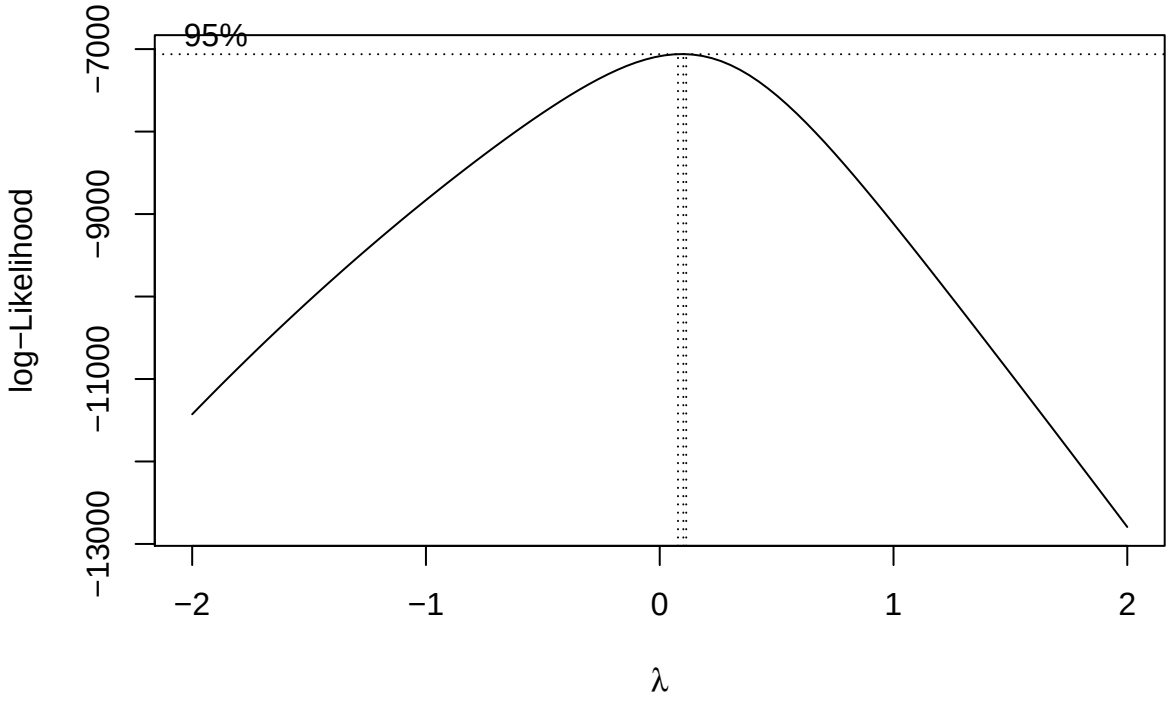
```
## labMitsubis     labNihon   labPoulenc  labSumitomo       labTNO
##    24.63683     13.18893     -4.14169     28.52520     16.56429
##      labWIL    labZeneca
##    10.05022     17.93047
```

```
library(MASS)
```

```
##
## Attaching package: 'MASS'
```

```
## The following object is masked from 'package:dplyr':
##
##     select
```

```
box =boxcox(lm1)
```

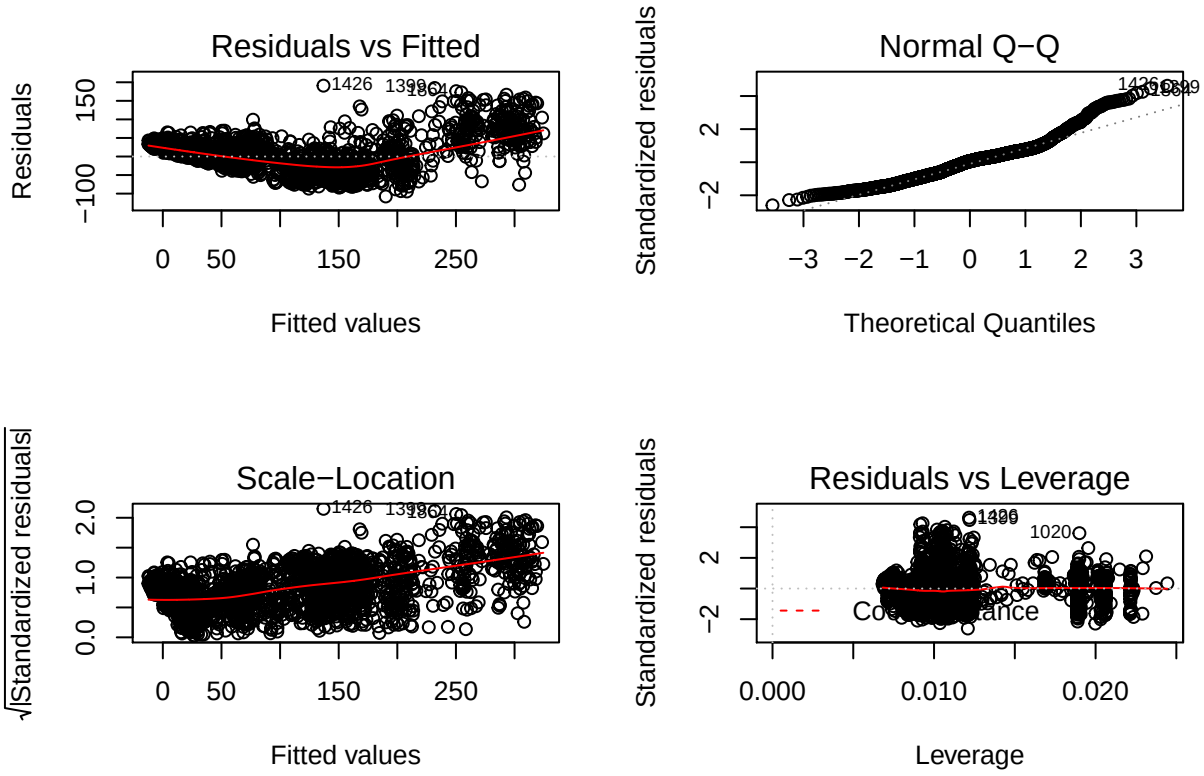



```
lm2 = lm(formula = log(uterus) ~ log(weight) + protocol + EE + ZM + lab, data = bioassay_lm)
summary(lm2)
```

```
##
## Call:
## lm(formula = log(uterus) ~ log(weight) + protocol + EE + ZM +
##     lab, data = bioassay_lm)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -1.38682 -0.16223  0.01173  0.16583  1.21149
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  1.321144   0.239602   5.514 3.85e-08 ***
## log(weight)  0.410375   0.058372   7.030 2.61e-12 ***
## protocolB    0.055004   0.014890   3.694 0.000225 ***
## protocolC    0.689389   0.083618   8.244 2.58e-16 ***
```

```
## protocolD    0.675012   0.085999   7.849 6.03e-15 ***
## EE0.01       0.002747   0.021776   0.126 0.899614
## EE0.03       0.012017   0.021606   0.556 0.578144
## EE0.1        0.131728   0.021388   6.159 8.44e-10 ***
## EE0.3        0.551201   0.021396  25.762  < 2e-16 ***
## EE1          1.061739   0.021438  49.527  < 2e-16 ***
## EE3          1.352063   0.021477  62.954  < 2e-16 ***
## EE10         1.451617   0.021571  67.294  < 2e-16 ***
## ZM0.1       -0.531428   0.024670 -21.541  < 2e-16 ***
## ZM1         -1.145005   0.024622 -46.504  < 2e-16 ***
## labBayer     0.457789   0.055245   8.286  < 2e-16 ***
## labBerlin    0.610866   0.057515  10.621  < 2e-16 ***
## labChungKor  0.762522   0.044567  17.109  < 2e-16 ***
## labCitfranc  0.559241   0.048950  11.425  < 2e-16 ***
## labCitijapa  0.445367   0.041829  10.647  < 2e-16 ***
## labDenmark   0.506016   0.051920   9.746  < 2e-16 ***
## labExxon     0.517897   0.050097  10.338  < 2e-16 ***
## labHatano    0.383445   0.040728   9.415  < 2e-16 ***
## labHuntingd -0.053061   0.053724  -0.988 0.323416
## labInEnvTox  0.455932   0.042501  10.728  < 2e-16 ***
## labKoreaPar  0.178793   0.046846   3.817 0.000138 ***
## labMitsubis  0.392970   0.040688   9.658  < 2e-16 ***
## labNihon     0.307153   0.040710   7.545 6.19e-14 ***
## labPoulenc   0.097765   0.051708   1.891 0.058768 .
## labSumitomo  0.464850   0.041551  11.187  < 2e-16 ***
## labTNO       0.533952   0.047525  11.235  < 2e-16 ***
## labWIL       0.380265   0.044646   8.517  < 2e-16 ***
## labZeneca    0.251125   0.041670   6.027 1.91e-09 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.273 on 2645 degrees of freedom
## Multiple R-squared:  0.8937, Adjusted R-squared:  0.8925
## F-statistic: 717.6 on 31 and 2645 DF,  p-value: < 2.2e-16
```

```
par(mfrow=c(2,2))
plot(lm1)
```



Frequentist Random Effect Model:

```
library(lme4)
```

```
## Loading required package: Matrix
```

```
##
## Attaching package: 'Matrix'
```

```
## The following object is masked from 'package:tidyr':
##
##     expand
```

```
randomeffect = lmer(log(uterus) ~ log(weight) + protocol + EE + ZM + (1+EE+ZM|lab), data = bioassay_lm)
```

```
## Warning in commonArgs(par, fn, control, environment()): maxfun < 10 *
## length(par)^2 is not recommended.
```

```
## Warning in optwrap(optimizer, devfun, getStart(start, rho$lower, rho$pp), :
## convergence code 1 from bobyqa: bobyqa -- maximum number of function
## evaluations exceeded
```

```
## Warning in commonArgs(par, fn, control, environment()): maxfun < 10 *
## length(par)^2 is not recommended.
```

```
## singular fit
```

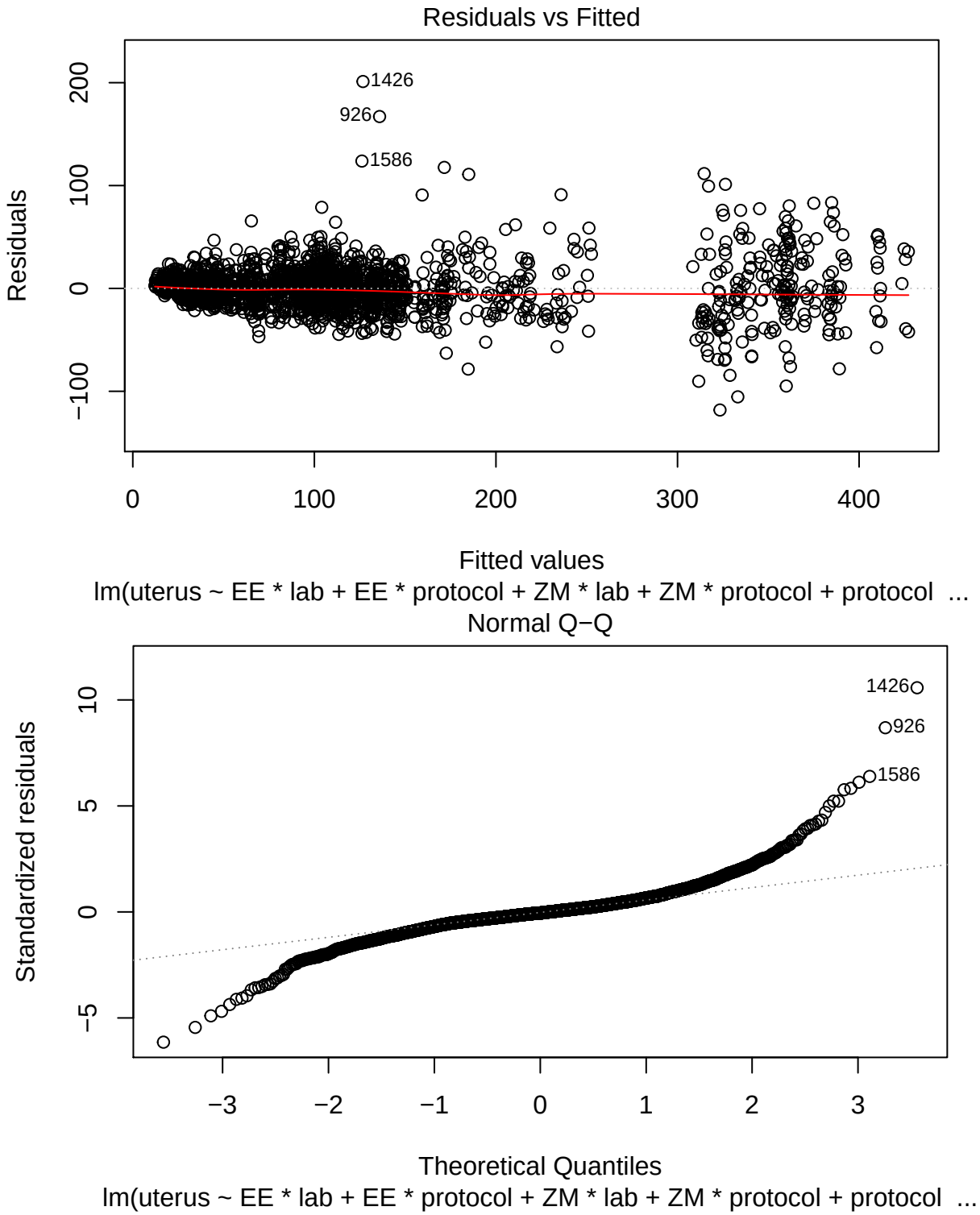
```
summary(randomeffect)
```

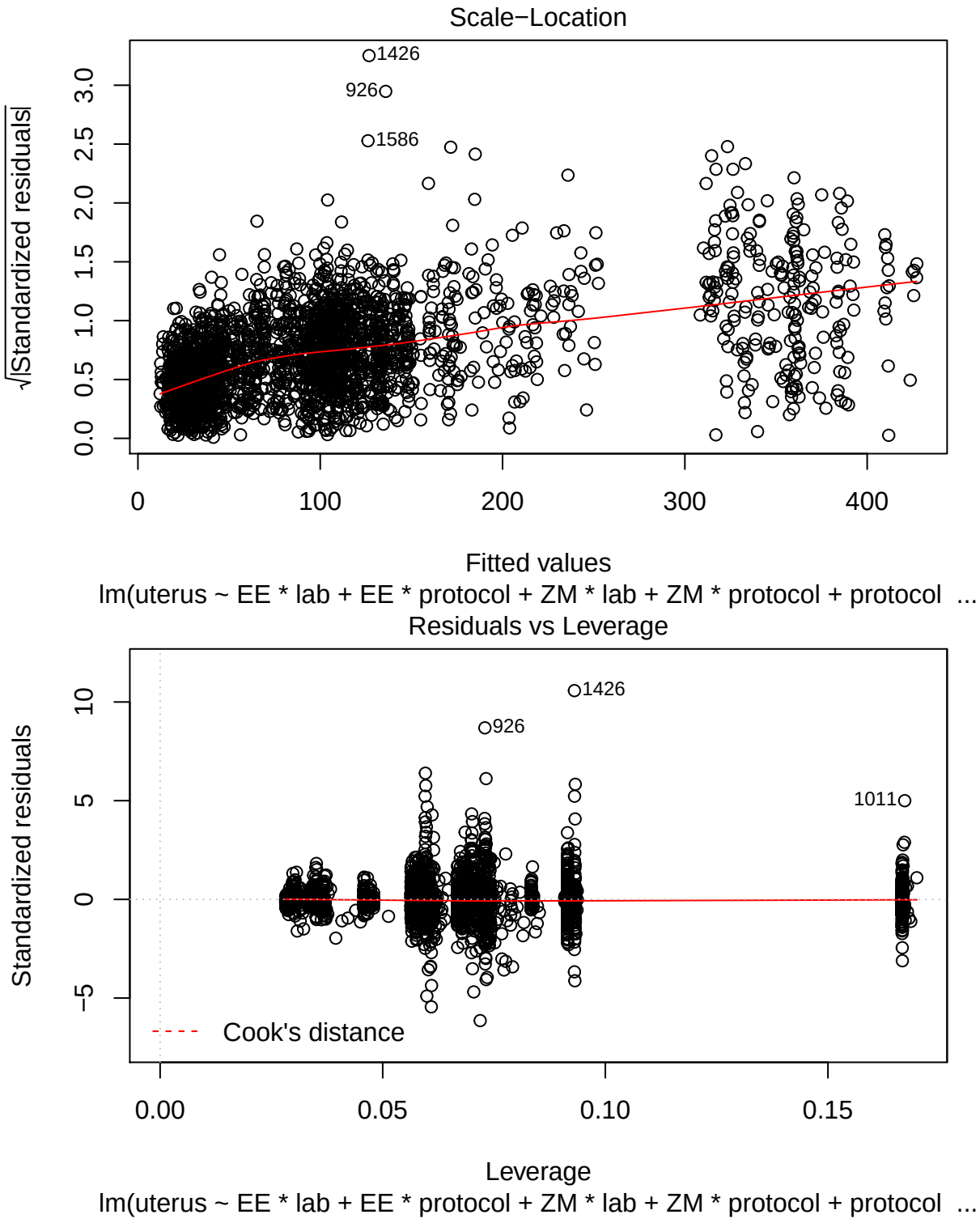
```
## Linear mixed model fit by REML ['lmerMod']
## Formula: log(uterus) ~ log(weight) + protocol + EE + ZM + (1 + EE + ZM |
##     lab)
##    Data: bioassay_lm
##
```

```
## REML criterion at convergence: 74.5
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -5.4143 -0.5782  0.0019  0.5717  5.4534
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  lab      (Intercept) 0.038505 0.19623
##           EE0.01      0.002410 0.04909  -0.13
##           EE0.03      0.003451 0.05874   0.52 -0.11
##           EE0.1       0.015031 0.12260   0.39 -0.89  0.55
##           EE0.3       0.094876 0.30802  -0.21 -0.76 -0.02  0.62
##           EE1         0.170537 0.41296  -0.34 -0.58 -0.11  0.41  0.94
##           EE3         0.045228 0.21267  -0.45 -0.26 -0.12  0.14  0.78
##           EE10        0.015602 0.12491  -0.62  0.27 -0.33 -0.41  0.35
##           ZM0.1       0.108467 0.32934   0.34  0.34  0.88  0.11 -0.28
##           ZM1         0.058895 0.24268   0.35  0.25  0.80  0.15 -0.52
##  Residual             0.053099 0.23043
##
##
##
##
##
##
##
##   0.94
##   0.62  0.84
##  -0.30 -0.16 -0.13
##  -0.53 -0.44 -0.40  0.80
##
## Number of obs: 2677, groups:  lab, 19
##
## Fixed effects:
##             Estimate Std. Error t value
## (Intercept)  1.62766    0.19575   8.315
## log(weight)  0.43491    0.04834   8.998
## protocolB    0.05597    0.01250   4.478
## protocolC    0.65373    0.06946   9.412
## protocolD    0.64037    0.07140   8.969
## EE0.01       0.02789    0.02172   1.284
## EE0.03       0.02528    0.02277   1.110
## EE0.1        0.11530    0.03376   3.416
## EE0.3        0.46623    0.07330   6.361
## EE1          0.95558    0.09684   9.868
## EE3          1.30993    0.05233  25.033
## EE10         1.43968    0.03423  42.062
## ZM0.1       -0.45946    0.07888  -5.825
## ZM1         -1.07974    0.05999 -17.999
##
## Correlation matrix not shown by default, as p = 14 > 12.
## Use print(x, correlation=TRUE)  or
##     vcov(x)        if you need it
```

```
## convergence code: 0
## singular fit
## maxfun < 10 * length(par)^2 is not recommended.
```

```
lm.full = lm(uterus~EE*lab+EE*protocol+ZM*lab+ZM*protocol+protocol+weight, data = bioassay)
plot(lm.full)
```





a.

Is the uterotrophic bioassay successful overall at identifying estrogenic effects of EE and anti- estrogenic effects of ZM? Do some labs fail to detect such effects? At what dose level of EE is there a change relative to the control and does this level vary across labs?

```r
anova(lm.full)
```

```
## Analysis of Variance Table
##
## Response: uterus
##               Df  Sum Sq Mean Sq  F value    Pr(>F)
## EE             7 6461242  923035 2314.192 < 2.2e-16 ***
## lab           18 2425580  134754  337.851 < 2.2e-16 ***
## protocol       3 7417598 2472533 6199.025 < 2.2e-16 ***
## ZM             2 2088738 1044369 2618.396 < 2.2e-16 ***
## weight         1  117187  117187  293.805 < 2.2e-16 ***
## EE:lab       123  872697    7095   17.788 < 2.2e-16 ***
## EE:protocol   21 1644774   78323  196.367 < 2.2e-16 ***
## lab:ZM        36  434688   12075   30.273 < 2.2e-16 ***
## protocol:ZM    6  635763  105960  265.659 < 2.2e-16 ***
## Residuals   2459  980793     399
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
coefs = summary(lm.full)$coefficients %>% data.frame()
colnames(coefs)=c("Estimate", "Std.Error", "t.value", "P.value")
kable(coefs)
```

	Estimate	Std.Error	t.value	P.value
(Intercept)	17.6921398	6.2283464	2.8405838	0.0045402
EE0.01	1.7701399	6.3709462	0.2778457	0.7811542
EE0.03	1.0378908	10.1359258	0.1023972	0.9184497
EE0.1	2.7432160	10.1361787	0.2706361	0.7866936
EE0.3	-1.2249771	10.1358912	-0.1208554	0.9038155
EE1	4.9154699	10.1358996	0.4849565	0.6277504
EE3	69.3115588	10.1360074	6.8381520	0.0000000
EE10	85.6371823	10.1363218	8.4485461	0.0000000
labBayer	13.5599357	8.3484811	1.6242399	0.1044528
labBerlin	5.1255856	8.3655611	0.6127008	0.5401309
labChungKor	16.9958608	7.3875081	2.3006216	0.0214963
labCitfranc	19.9135236	8.3366042	2.3886853	0.0169838
labCitijapa	13.4429984	7.0580652	1.9046294	0.0569448
labDenmark	9.5877157	8.7221893	1.0992327	0.2717742
labExxon	15.6604413	10.1361133	1.5450144	0.1224714
labHatano	11.9498140	6.9083411	1.7297661	0.0837976
labHuntingd	-8.1394636	9.0112917	-0.9032516	0.3664809
labInEnvTox	4.7193764	6.9572738	0.6783370	0.4976219
labKoreaPar	-2.4460044	7.6562213	-0.3194793	0.7493902
labMitsubis	11.9576775	6.9093842	1.7306430	0.0836409
labNihon	5.9004474	6.9097671	0.8539286	0.3932278
labPoulenc	-3.8767398	8.3457355	-0.4645175	0.6423182
labSumitomo	10.7102334	7.0571585	1.5176411	0.1292335
labTNO	5.1244311	7.4554856	0.6873370	0.4919352
labWIL	6.7280809	7.3900800	0.9104206	0.3626900
labZeneca	-4.0076574	7.0778683	-0.5662238	0.5712933
protocolB	-2.1610930	2.5551149	-0.8457909	0.3977517
protocolC	57.4966953	5.5324392	10.3926483	0.0000000
protocolD	47.8797880	6.3029055	7.5964629	0.0000000
ZM0.1	-44.2666292	11.5305487	-3.8390739	0.0001266

	Estimate	Std.Error	t.value	P.value
ZM1	-68.4672254	11.5305183	-5.9379140	0.0000000
weight	0.0983238	0.0275887	3.5639120	0.0003723
EE0.1:labBayer	-1.9413540	14.2285737	-0.1364405	0.8914842
EE0.3:labBayer	-1.0759172	14.2286635	-0.0756162	0.9397306
EE1:labBayer	2.4327603	14.2289689	0.1709724	0.8642596
EE3:labBayer	-28.2053769	14.2285472	-1.9823090	0.0475558
EE10:labBayer	13.3718307	14.2288133	0.9397713	0.3474272
EE0.01:labBerlin	-0.8718434	11.8448246	-0.0736054	0.9413303
EE0.03:labBerlin	2.9065320	14.2285241	0.2042750	0.8381555
EE0.1:labBerlin	-2.7973588	14.2292670	-0.1965919	0.8441631
EE0.3:labBerlin	15.6309460	14.2286601	1.0985536	0.2720704
EE1:labBerlin	49.4838691	14.2285209	3.4777943	0.0005143
EE3:labBerlin	36.1929758	14.2286878	2.5436622	0.0110304
EE10:labBerlin	5.9541129	14.2302966	0.4184110	0.6756832
EE0.01:labChungKor	-4.4227978	9.2334220	-0.4789988	0.6319821
EE0.03:labChungKor	3.6542317	12.5489789	0.2911975	0.7709248
EE0.1:labChungKor	25.0578867	12.5492986	1.9967560	0.0459618
EE0.3:labChungKor	29.9631938	12.5490889	2.3876788	0.0170302
EE1:labChungKor	33.4866563	12.5490107	2.6684698	0.0076698
EE3:labChungKor	5.8794592	12.5491838	0.4685133	0.6394591
EE10:labChungKor	-13.1302296	12.5500788	-1.0462269	0.2955591
EE0.01:labCitfranc	-5.4673561	11.8451179	-0.4615704	0.6444302
EE0.03:labCitfranc	2.1025749	14.2285222	0.1477718	0.8825350
EE0.1:labCitfranc	-4.7655344	14.2287442	-0.3349230	0.7377117
EE0.3:labCitfranc	4.4900701	14.2285349	0.3155680	0.7523572
EE1:labCitfranc	15.3965133	14.2285406	1.0820866	0.2793201
EE3:labCitfranc	-11.4516245	14.2285356	-0.8048351	0.4209927
EE10:labCitfranc	12.3238231	14.2286889	0.8661250	0.3865061
EE0.01:labCitijapa	-3.0235543	8.1536667	-0.3708214	0.7108025
EE0.03:labCitijapa	-4.5859463	11.9717926	-0.3830626	0.7017064
EE0.1:labCitijapa	-7.0987885	11.9718389	-0.5929572	0.5532643
EE0.3:labCitijapa	-3.2750500	11.9716979	-0.2735660	0.7844411
EE1:labCitijapa	35.0612365	11.9718333	2.9286439	0.0034357
EE3:labCitijapa	5.0500990	11.9716950	0.4218366	0.6731812
EE10:labCitijapa	10.5680912	11.9720931	0.8827271	0.3774700
EE0.01:labDenmark	-2.1156506	11.8184115	-0.1790131	0.8579422
EE0.03:labDenmark	-3.8716071	14.8992290	-0.2598528	0.7949990
EE0.1:labDenmark	-5.4275941	14.8990603	-0.3642910	0.7156720
EE0.3:labDenmark	27.6907502	14.8990352	1.8585600	0.0632089
EE1:labDenmark	40.2481584	14.8993790	2.7013313	0.0069536
EE3:labDenmark	8.8724601	14.8991321	0.5955018	0.5515629
EE10:labDenmark	-2.3083513	14.9025781	-0.1548961	0.8769159
EE0.01:labExxon	5.2408100	13.1734606	0.3978309	0.6907894
EE0.03:labExxon	0.6638228	15.3521914	0.0432396	0.9655140
EE0.1:labExxon	-0.3674801	15.3526063	-0.0239360	0.9809056
EE0.3:labExxon	9.4632641	15.3521774	0.6164119	0.5376798
EE1:labExxon	11.9086272	15.3521859	0.7756959	0.4380032
EE3:labExxon	5.4879948	15.3526675	0.3574620	0.7207767
EE10:labExxon	14.6811231	15.3524493	0.9562724	0.3390286
EE0.01:labHatano	-3.1391717	7.7623171	-0.4044117	0.6859452
EE0.03:labHatano	-3.6455000	11.7106696	-0.3112973	0.7556010
EE0.1:labHatano	2.0072571	11.7085264	0.1714355	0.8638954

	Estimate	Std.Error	t.value	P.value
EE0.3:labHatano	2.9241566	11.7085297	0.2497458	0.8028048
EE1:labHatano	25.9776627	11.7086219	2.2186781	0.0265996
EE3:labHatano	14.2692412	11.7086377	1.2186935	0.2230774
EE10:labHatano	23.8552606	11.7386011	2.0322064	0.0422400
EE0.01:labHuntingd	7.8784060	11.8975318	0.6621883	0.5079126
EE0.03:labHuntingd	-5.1408169	15.0873643	-0.3407366	0.7333310
EE0.1:labHuntingd	-32.8815501	15.0899176	-2.1790411	0.0294232
EE0.3:labHuntingd	-91.0178211	15.0897691	-6.0317570	0.0000000
EE1:labHuntingd	-151.3054403	15.0872126	-10.0287206	0.0000000
EE3:labHuntingd	-101.1249020	15.0935628	-6.6998695	0.0000000
EE10:labHuntingd	-5.2949207	15.0890160	-0.3509123	0.7256842
EE0.01:labInEnvTox	-5.5062872	7.7618711	-0.7094020	0.4781423
EE0.03:labInEnvTox	-2.5009443	11.7105266	-0.2135638	0.8309050
EE0.1:labInEnvTox	-0.3415523	11.7096969	-0.0291683	0.9767327
EE0.3:labInEnvTox	8.1049832	11.7085361	0.6922286	0.4888592
EE1:labInEnvTox	35.7979406	11.7087305	3.0573716	0.0022569
EE3:labInEnvTox	5.8104777	11.7090811	0.4962369	0.6197717
EE10:labInEnvTox	-5.1453068	11.7092036	-0.4394241	0.6603928
EE0.01:labKoreaPar	-4.5648235	9.2159706	-0.4953166	0.6204209
EE0.03:labKoreaPar	-9.0478787	13.0047842	-0.6957346	0.4866608
EE0.1:labKoreaPar	-13.5687159	13.0051963	-1.0433303	0.2968979
EE0.3:labKoreaPar	-8.2118046	13.0047840	-0.6314449	0.5278084
EE1:labKoreaPar	32.4992463	13.0049905	2.4989827	0.0125198
EE3:labKoreaPar	-5.6884006	13.0054179	-0.4373870	0.6618691
EE10:labKoreaPar	10.6822373	13.0061162	0.8213242	0.4115413
EE0.01:labMitsubis	-6.9672860	7.7620864	-0.8976048	0.3694842
EE0.03:labMitsubis	-3.6538049	11.7266100	-0.3115824	0.7553844
EE0.1:labMitsubis	-2.4379617	11.7085261	-0.2082211	0.8350736
EE0.3:labMitsubis	10.1457484	11.7086923	0.8665142	0.3862928
EE1:labMitsubis	23.9905950	11.7092995	2.0488497	0.0405827
EE3:labMitsubis	12.0136442	11.7089145	1.0260254	0.3049805
EE10:labMitsubis	10.1939679	11.7086648	0.8706345	0.3840387
EE0.01:labNihon	1.1342292	7.7622619	0.1461210	0.8838379
EE0.03:labNihon	-6.8542963	11.7105338	-0.5853103	0.5583928
EE0.1:labNihon	-11.0475122	11.7086265	-0.9435361	0.3454994
EE0.3:labNihon	-4.3192633	11.7087772	-0.3688911	0.7122407
EE1:labNihon	22.3176093	11.7085636	1.9060928	0.0567546
EE3:labNihon	16.6960124	11.7085405	1.4259687	0.1540043
EE10:labNihon	16.7156938	11.7087850	1.4276198	0.1535283
EE0.01:labPoulenc	-2.6767783	11.8448384	-0.2259869	0.8212304
EE0.03:labPoulenc	-1.0819782	14.2285209	-0.0760429	0.9393911
EE0.1:labPoulenc	-2.1250690	14.2286472	-0.1493514	0.8812886
EE0.3:labPoulenc	15.6299768	14.2286052	1.0984897	0.2720982
EE1:labPoulenc	31.5497164	14.2285209	2.2173574	0.0266898
EE3:labPoulenc	-17.8746600	14.2285859	-1.2562499	0.2091447
EE10:labPoulenc	-25.6318658	14.2287762	-1.8014104	0.0717607
EE0.01:labSumitomo	-0.7795783	8.1534741	-0.0956130	0.9238357
EE0.03:labSumitomo	-1.5687737	11.9717781	-0.1310393	0.8957549
EE0.1:labSumitomo	-6.9354396	11.9718635	-0.5793116	0.5624320
EE0.3:labSumitomo	11.7092981	11.9717402	0.9780782	0.3281319
EE1:labSumitomo	42.0312958	11.9716966	3.5108888	0.0004546
EE3:labSumitomo	24.4538517	11.9717859	2.0426235	0.0411962

	Estimate	Std.Error	t.value	P.value
EE10:labSumitomo	35.6596086	11.9720722	2.9785661	0.0029243
EE0.01:labTNO	0.1409306	9.2719005	0.0151998	0.9878740
EE0.03:labTNO	-0.9350942	12.5834691	-0.0743113	0.9407687
EE0.1:labTNO	-5.5913465	12.5836286	-0.4443350	0.6568395
EE0.3:labTNO	2.7513260	12.5835230	0.2186451	0.8269446
EE1:labTNO	32.7382800	12.5835389	2.6016751	0.0093326
EE3:labTNO	10.9601235	12.5835070	0.8709912	0.3838440
EE10:labTNO	20.5192902	12.5849485	1.6304628	0.1031318
EE0.01:labWIL	2.3879433	9.2328247	0.2586363	0.7959375
EE0.03:labWIL	-0.9964710	12.5489507	-0.0794067	0.9367156
EE0.1:labWIL	1.5719326	12.5495817	0.1252578	0.9003297
EE0.3:labWIL	-0.5850968	12.5490251	-0.0466249	0.9628160
EE1:labWIL	13.0474996	12.5490457	1.0397205	0.2985720
EE3:labWIL	-12.0028171	12.5493560	-0.9564488	0.3389395
EE10:labWIL	4.3168054	12.5506409	0.3439510	0.7309125
EE0.03:labZeneca	0.2451555	11.9717933	0.0204778	0.9836639
EE0.1:labZeneca	0.1782602	11.9720517	0.0148897	0.9881214
EE0.3:labZeneca	13.2683860	11.9717127	1.1083114	0.2678357
EE1:labZeneca	21.7897069	11.9717082	1.8201001	0.0688653
EE3:labZeneca	-23.5535783	11.9719315	-1.9674000	0.0492494
EE10:labZeneca	-16.8965915	11.9726142	-1.4112700	0.1582915
EE0.01:protocolB	1.1902964	4.4193150	0.2693396	0.7876910
EE0.03:protocolB	3.5418537	4.4193120	0.8014491	0.4229491
EE0.1:protocolB	7.5900388	4.4193228	1.7174665	0.0860199
EE0.3:protocolB	35.0978767	4.4193110	7.9419340	0.0000000
EE1:protocolB	58.2124603	4.4193491	13.1721796	0.0000000
EE3:protocolB	34.4012138	4.4193376	7.7842466	0.0000000
EE10:protocolB	17.5737941	4.4312030	3.9659194	0.0000752
EE0.01:protocolC	-0.3219158	5.0172722	-0.0641615	0.9488468
EE0.03:protocolC	2.7235600	5.0172696	0.5428371	0.5872912
EE0.1:protocolC	16.8961376	5.0181550	3.3670020	0.0007716
EE0.3:protocolC	100.1908816	5.0179722	19.9664084	0.0000000
EE1:protocolC	186.2703041	5.0226183	37.0862953	0.0000000
EE3:protocolC	169.9677193	5.0320482	33.7770454	0.0000000
EE10:protocolC	157.5051103	5.0391674	31.2561773	0.0000000
EE0.01:protocolD	6.4555202	6.3706594	1.0133206	0.3110068
EE0.03:protocolD	4.8354220	6.4292086	0.7521022	0.4520616
EE0.1:protocolD	31.1032766	6.3778672	4.8767520	0.0000011
EE0.3:protocolD	140.9528162	6.3802058	22.0922054	0.0000000
EE1:protocolD	230.4597903	6.4081260	35.9636793	0.0000000
EE3:protocolD	208.0722058	6.4268844	32.3752835	0.0000000
EE10:protocolD	216.8698781	6.4449178	33.6497509	0.0000000
labBayer:ZM0.1	50.8815276	16.3068064	3.1202632	0.0018279
labBerlin:ZM0.1	27.7245810	16.3066116	1.7002049	0.0892188
labChungKor:ZM0.1	57.6875289	14.3503878	4.0199282	0.0000600
labCitfranc:ZM0.1	30.2092368	16.3066650	1.8525699	0.0640638
labCitijapa:ZM0.1	31.7989098	13.6778097	2.3248539	0.0201608
labDenmark:ZM0.1	23.1363620	17.0854082	1.3541592	0.1758100
labExxon:ZM0.1	23.0558838	16.3068879	1.4138739	0.1575255
labHatano:ZM0.1	8.9988335	13.3922313	0.6719443	0.5016823
labHuntingd:ZM0.1	72.4267174	17.3109743	4.1838614	0.0000297
labInEnvTox:ZM0.1	23.3265475	13.3699157	1.7447041	0.0811613

	Estimate	Std.Error	t.value	P.value
labKoreaPar:ZM0.1	16.1575276	14.8832064	1.0856214	0.2777529
labMitsubis:ZM0.1	13.2488798	13.3699161	0.9909471	0.3218089
labNihon:ZM0.1	12.5911189	13.3699609	0.9417469	0.3464148
labPoulenc:ZM0.1	49.0120298	16.3066112	3.0056539	0.0026769
labSumitomo:ZM0.1	30.8721871	13.6778934	2.2570864	0.0240901
labTNO:ZM0.1	77.4752572	14.3503263	5.3988499	0.0000001
labWIL:ZM0.1	38.1845683	14.3502884	2.6608921	0.0078441
labZeneca:ZM0.1	77.9483444	13.6782162	5.6987215	0.0000000
labBayer:ZM1	32.7808940	16.3066168	2.0102817	0.0445104
labBerlin:ZM1	-2.2204654	16.3066221	-0.1361696	0.8916984
labChungKor:ZM1	33.0188857	14.3504195	2.3009004	0.0214806
labCitfranc:ZM1	12.7381194	16.3066277	0.7811621	0.4347824
labCitijapa:ZM1	7.7400766	13.6768691	0.5659246	0.5714967
labDenmark:ZM1	8.2138615	17.0853771	0.4807539	0.6307342
labExxon:ZM1	-5.2104660	16.3067300	-0.3195286	0.7493529
labHatano:ZM1	0.3058017	13.3696779	0.0228728	0.9817536
labHuntingd:ZM1	114.0565353	17.3048639	6.5910103	0.0000000
labInEnvTox:ZM1	10.2387909	13.3696378	0.7658241	0.4438545
labKoreaPar:ZM1	40.0313061	14.8813003	2.6900409	0.0071926
labMitsubis:ZM1	-5.9903757	13.3696378	-0.4480582	0.6541507
labNihon:ZM1	-4.3205526	13.3696532	-0.3231612	0.7466007
labPoulenc:ZM1	29.6033149	16.3066327	1.8154156	0.0695818
labSumitomo:ZM1	-7.6991541	13.6769161	-0.5629306	0.5735335
labTNO:ZM1	22.6384857	14.3502739	1.5775647	0.1147943
labWIL:ZM1	29.8051524	14.3502739	2.0769745	0.0379075
labZeneca:ZM1	44.7881960	13.6769129	3.2747299	0.0010723
protocolB:ZM0.1	-61.0363994	5.0994169	-11.9692900	0.0000000
protocolC:ZM0.1	-158.3876845	5.8154616	-27.2356168	0.0000000
protocolD:ZM0.1	-183.5812617	7.3793450	-24.8777177	0.0000000
protocolB:ZM1	-53.8649790	5.0993766	-10.5630517	0.0000000
protocolC:ZM1	-171.3005189	5.7964359	-29.5527322	0.0000000
protocolD:ZM1	-217.1910191	7.3755330	-29.4475015	0.0000000

```
t.test(lm.obj = lm.full, str.ee = "EE", str.lab = "lab", str.ori = "lab") %>%
  kable(.,caption = "T-test of EE across labs")
t.test(lm.obj = lm.full, str.ee = "ZM", str.lab = "lab", str.ori = "lab") %>%
  kable(.,caption = "T-test of EE across labs")
```

b.

Does the dose response vary across labs? If so, are there certain labs that stand out as being different?

See tables in a.

c.

Do the protocols differ in their sensitivity to detecting estrogenic and anti-estrogenic effects? If so, is there one protocol that can be recommended?

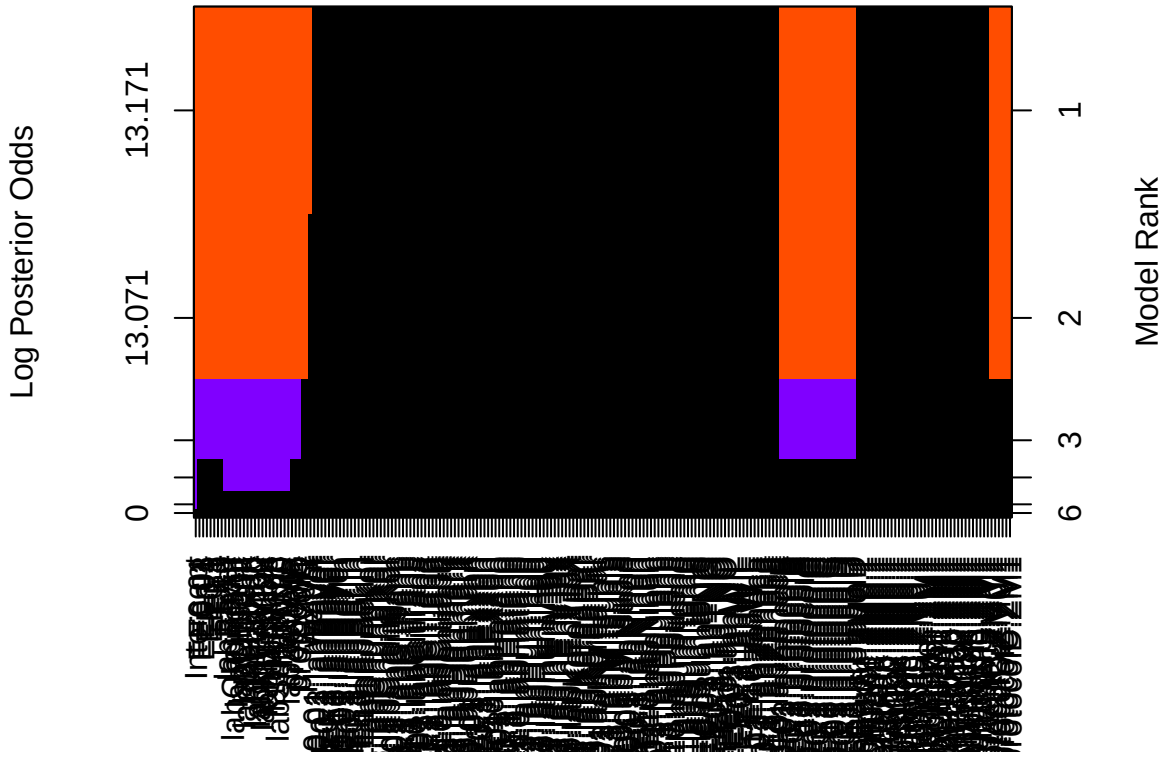
See tables in a.

Model Part II

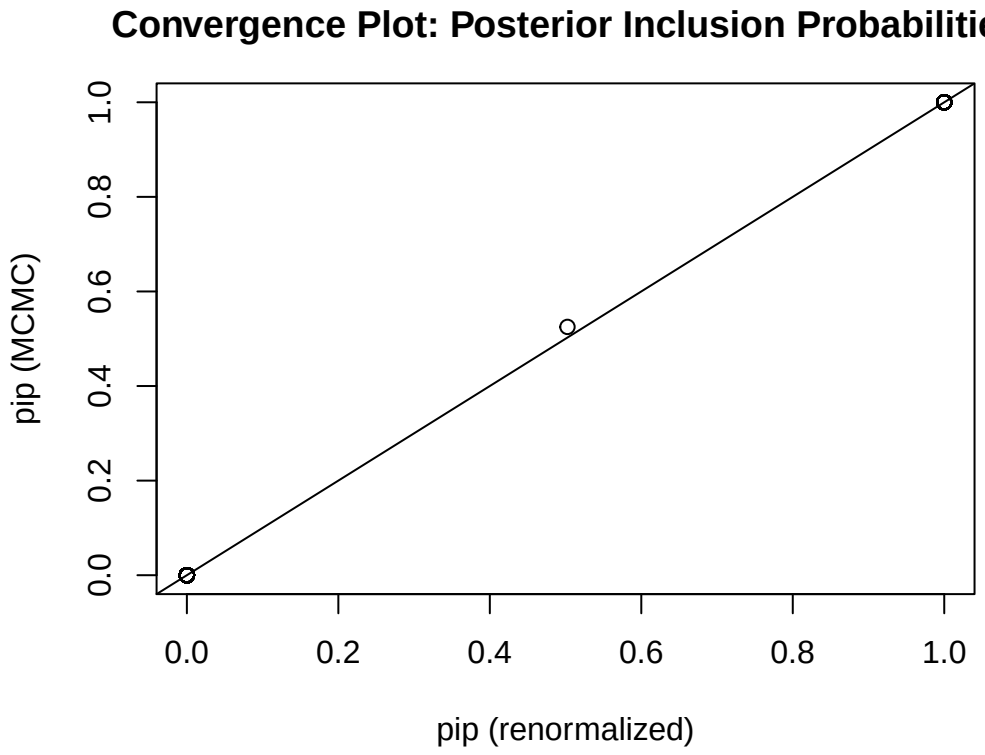
```
n = nrow(bioassay)
p = ncol(model.matrix(lm.full)) - 1

bas1 = bas.lm(uterus~EE*lab+EE*protocol+ZM*lab+ZM*protocol+protocol+weight,
              data = bioassay,
              prior = "hyper-g-n",
              alpha = n,
              method = "MCMC",
              MCMC.iterations = 10^6)
```

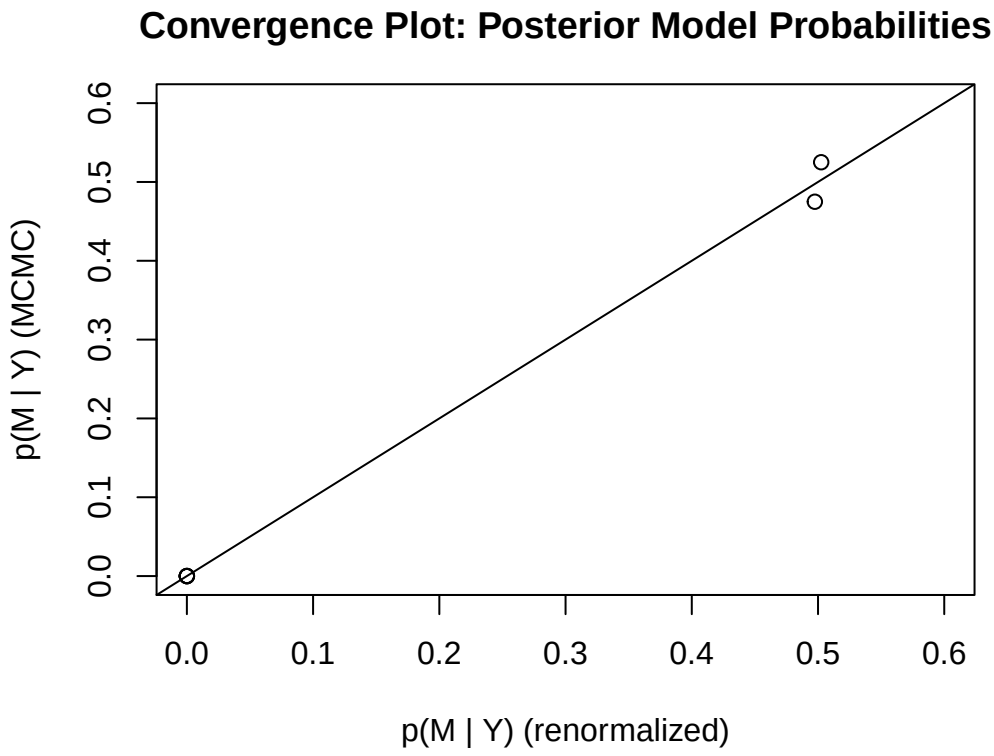
```
image(bas1)
```




```
diagnostics(bas1, type = "pip")
```



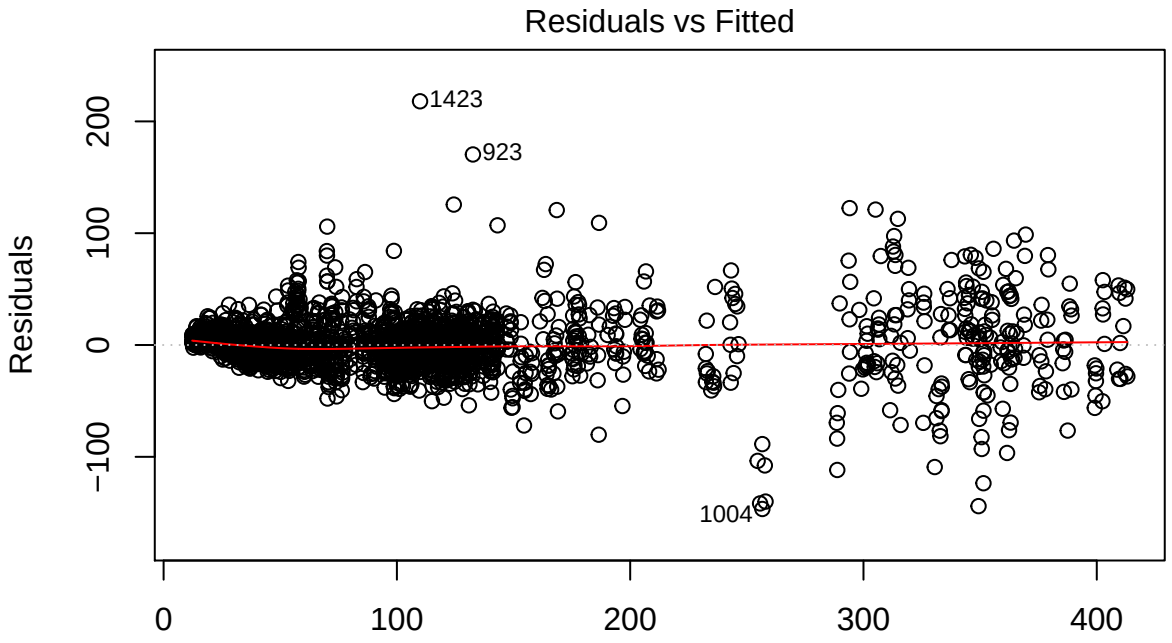

```
diagnostics(bas1, type = "model")
```

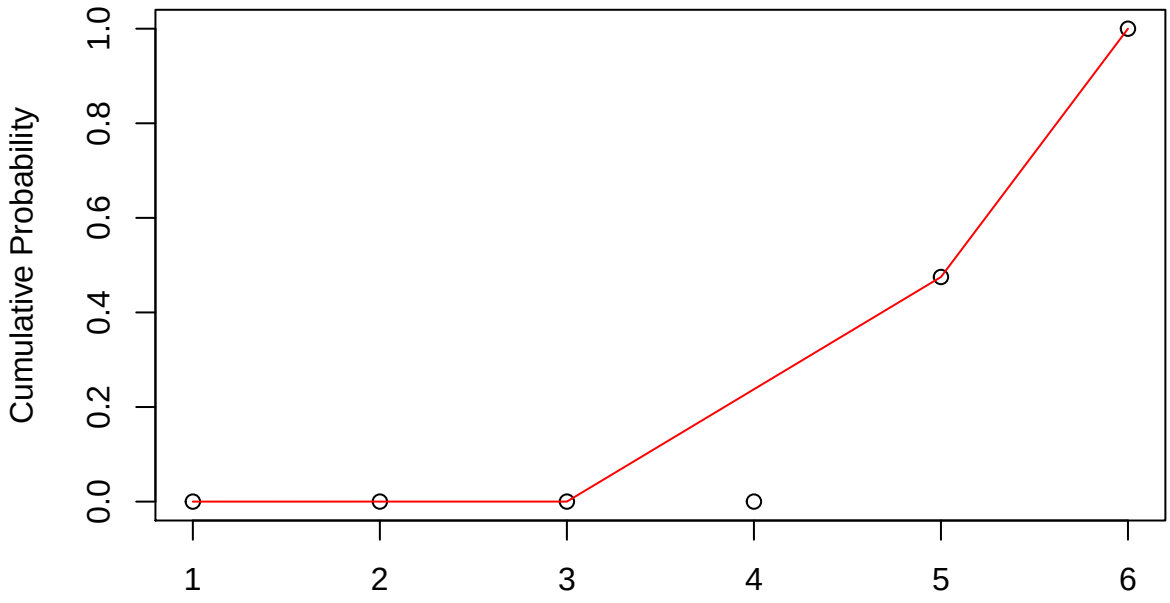


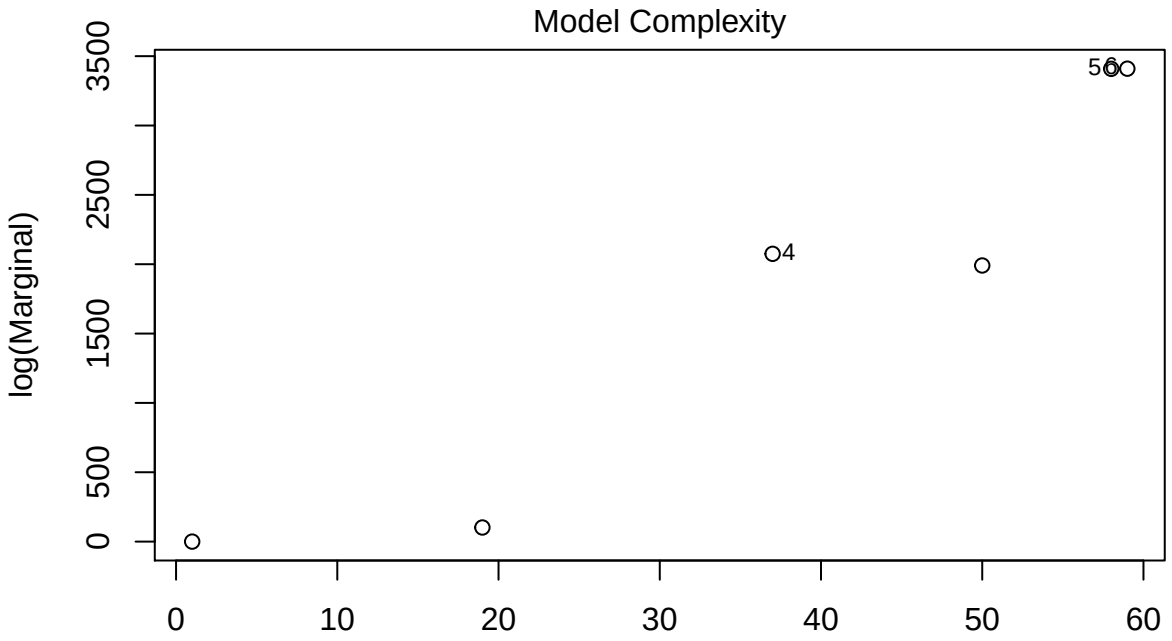
a.

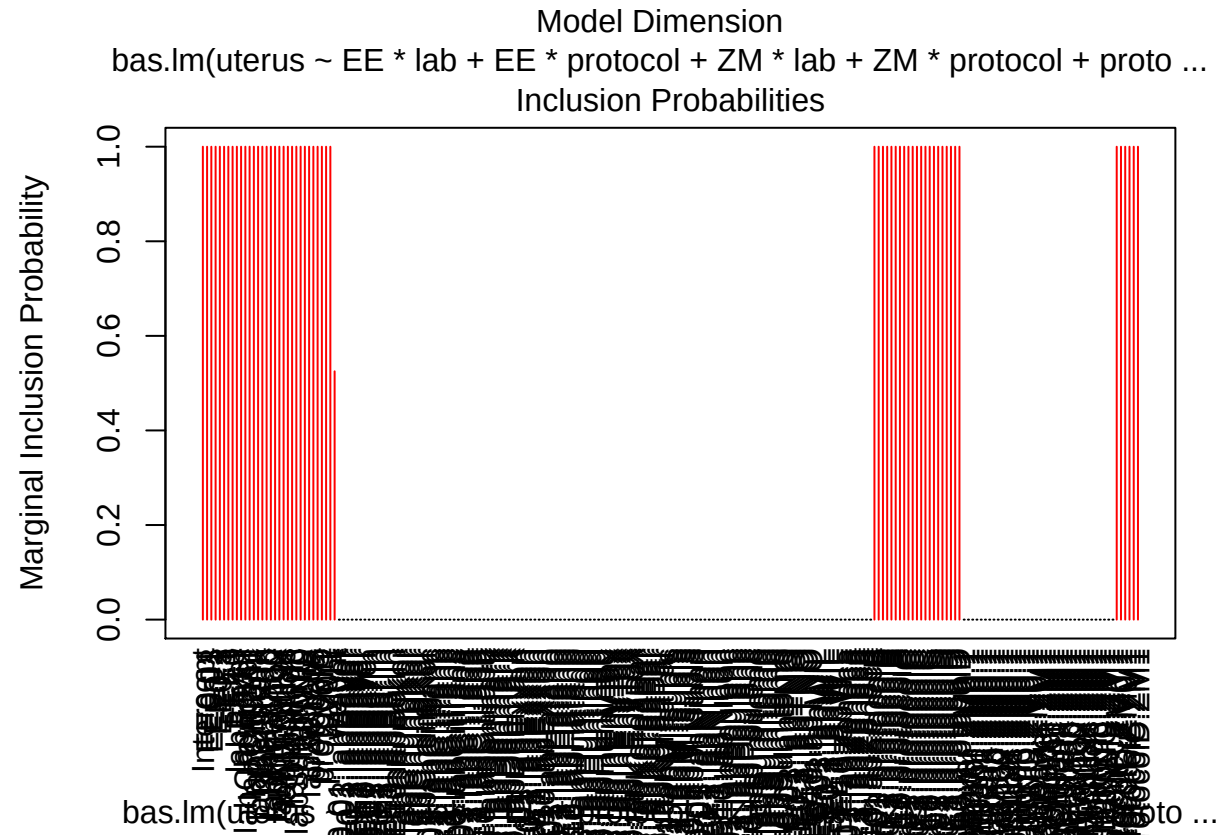
Is the uterotrophic bioassay successful overall at identifying estrogenic effects of EE and anti- estrogenic effects of ZM? Do some labs fail to detect such effects? At what dose level of EE is there a change relative to the control and does this level vary across labs?

```
plot(bas1)
```

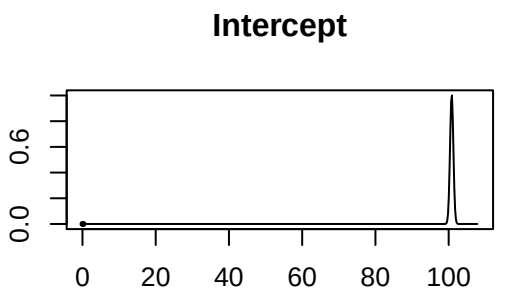

Residuals vs Fitted
Residuals
1423
923
1004
200
100
0
−100
0
100
200
300
400
Predictions under BMA
bas.lm(uterus ~ EE * lab + EE * protocol + ZM * lab + ZM * protocol + proto ...

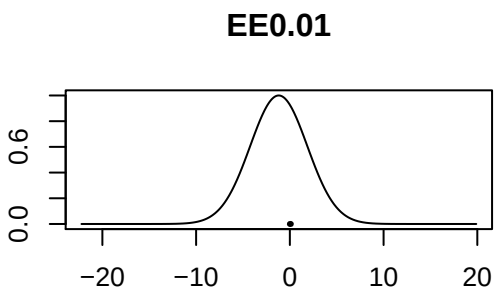

Model Probabilities
Cumulative Probability
0.0
0.2
0.4
0.6
0.8
1.0
1
2
3
4
5
6
Model Search Order
bas.lm(uterus ~ EE * lab + EE * protocol + ZM * lab + ZM * protocol + proto ...






```
par(mfrow=c(2,2))
plot(coef(bas1), ask=F)
```


Intercept
0.0
0.6
0
20
40
60
80
100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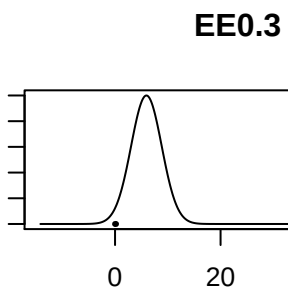
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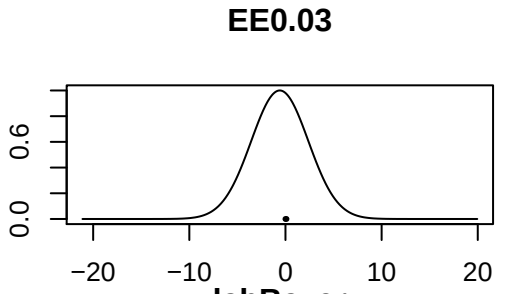
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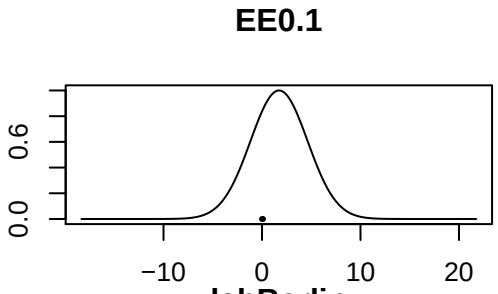
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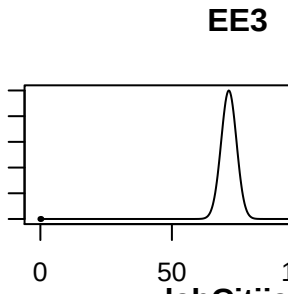
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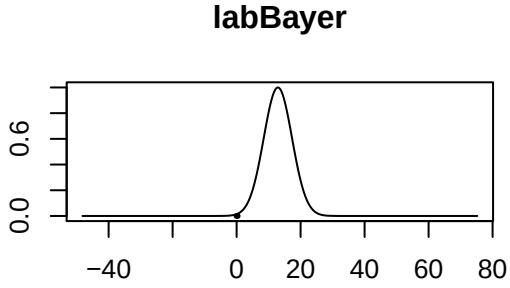
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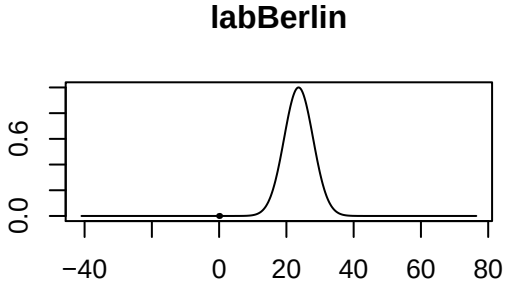
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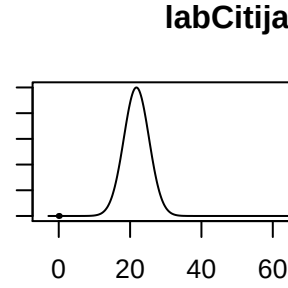
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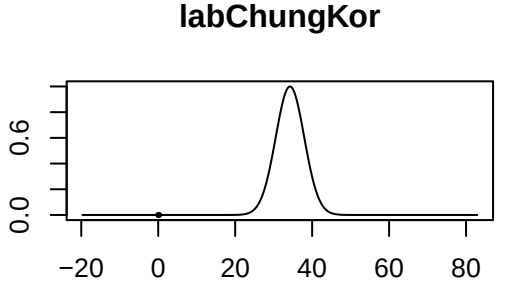
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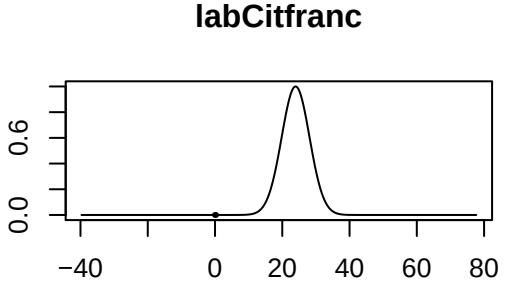
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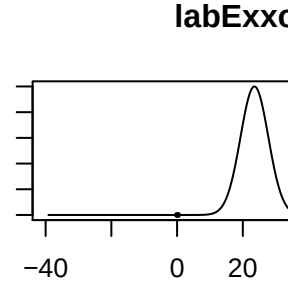
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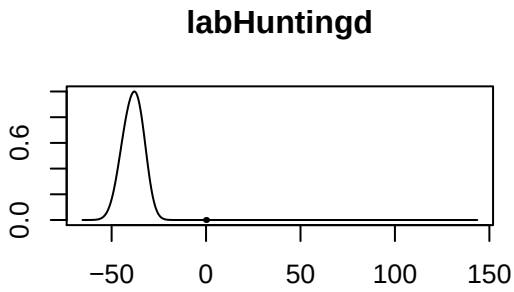
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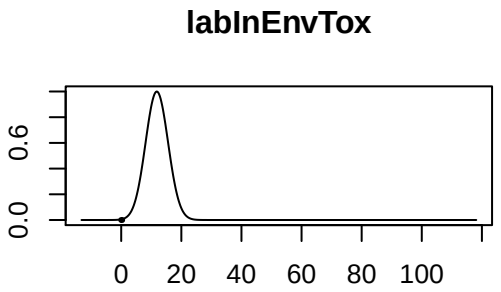
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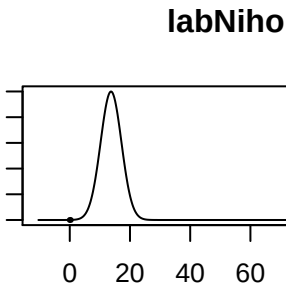
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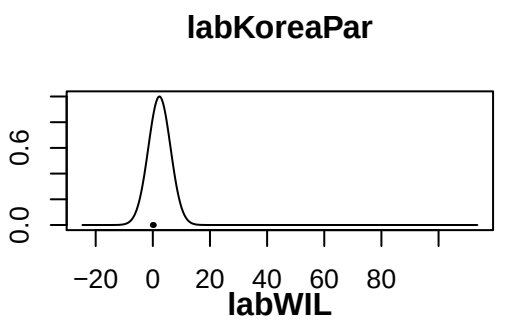
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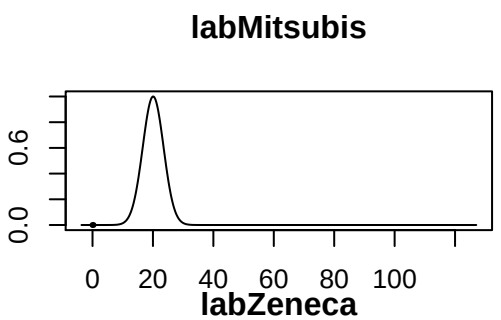
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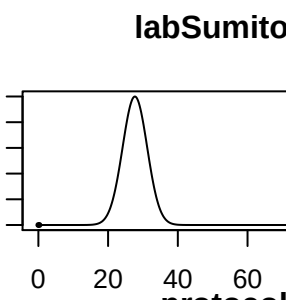
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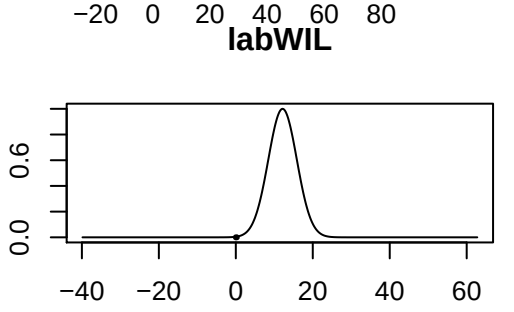
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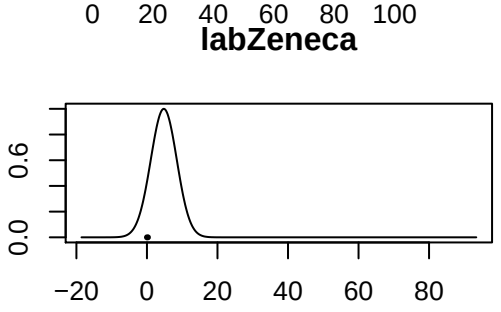
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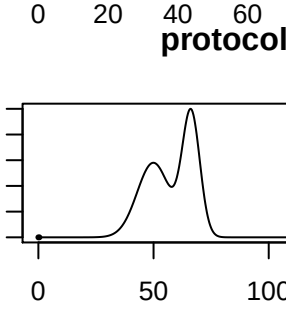
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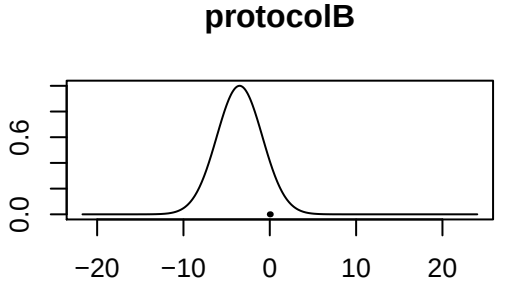
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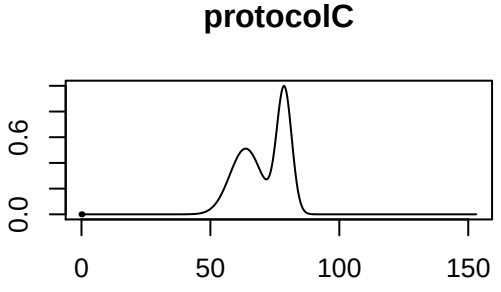
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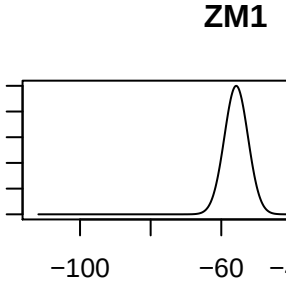
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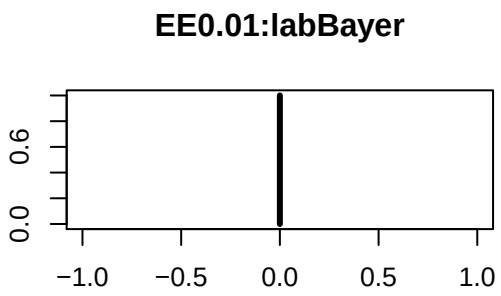
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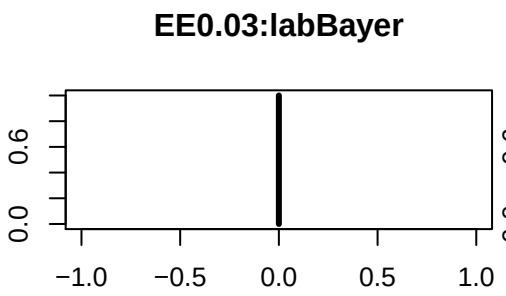
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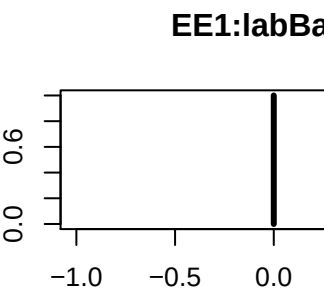
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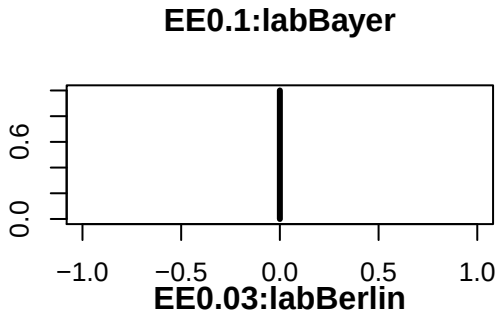
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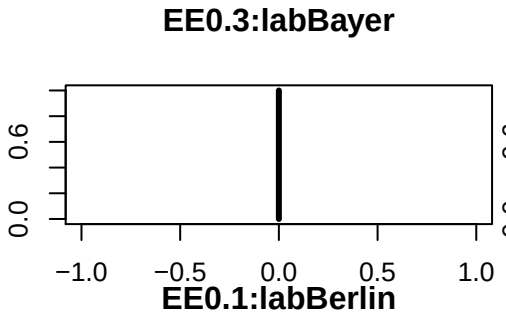
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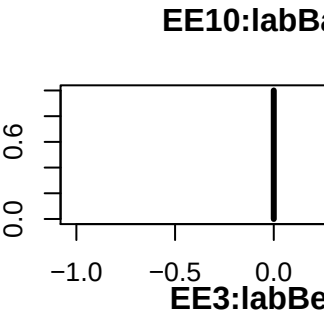
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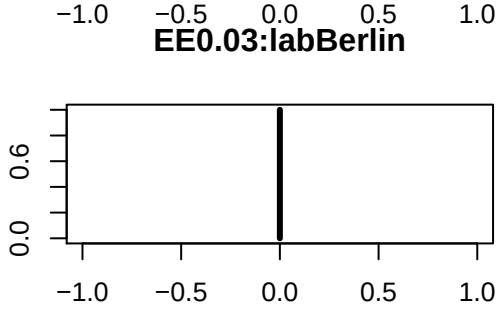
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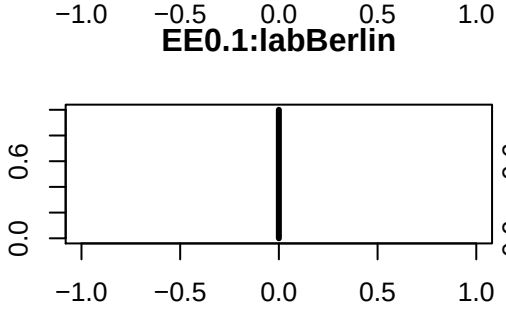
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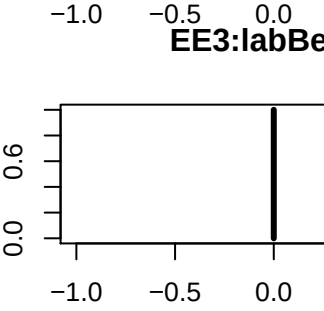
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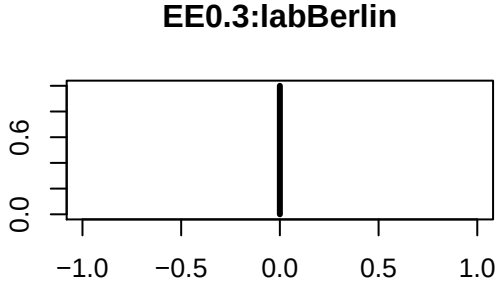
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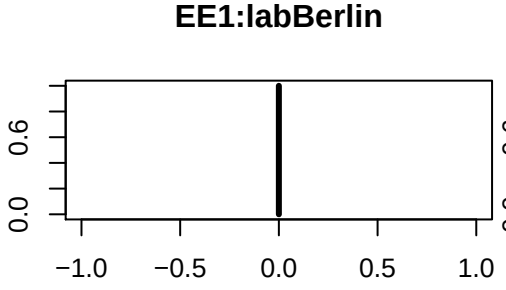
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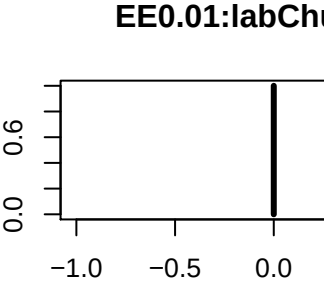
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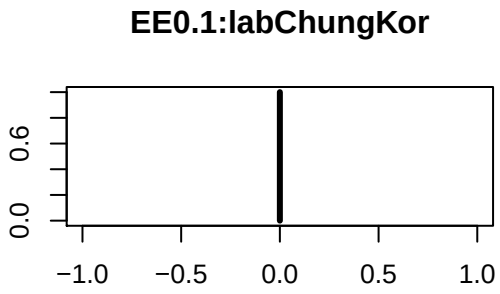
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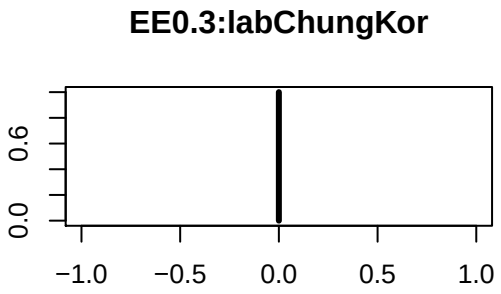
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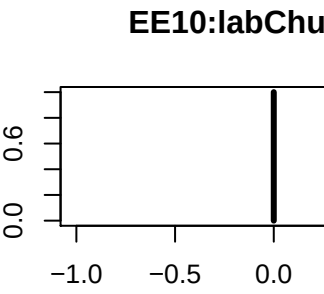
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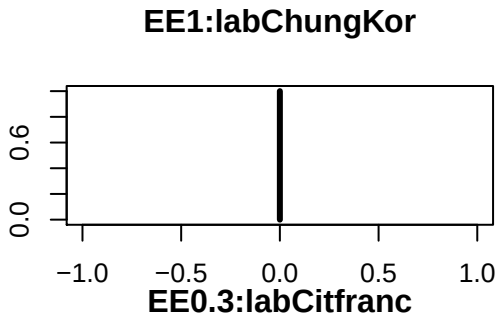
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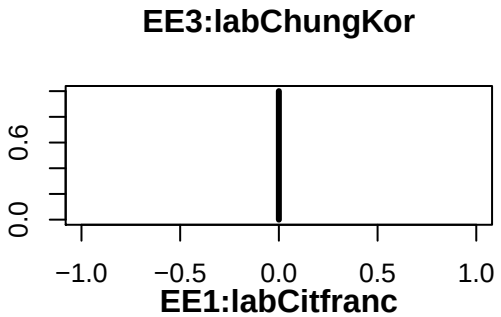
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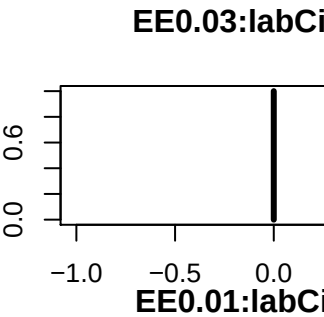
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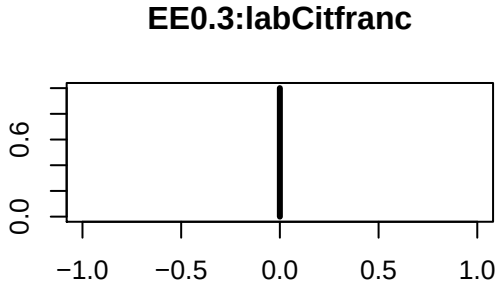
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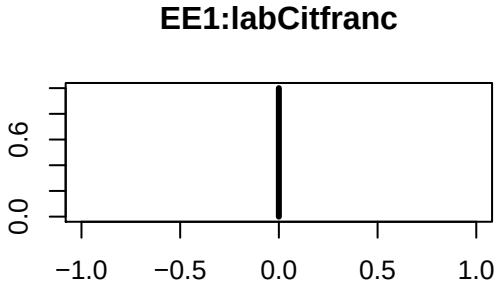
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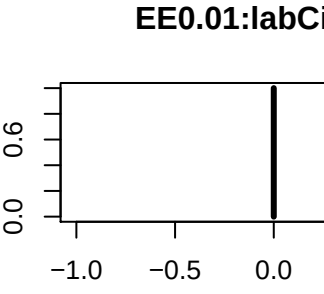
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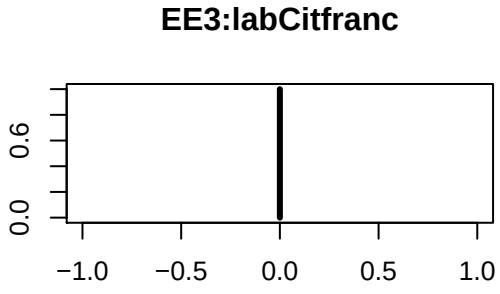
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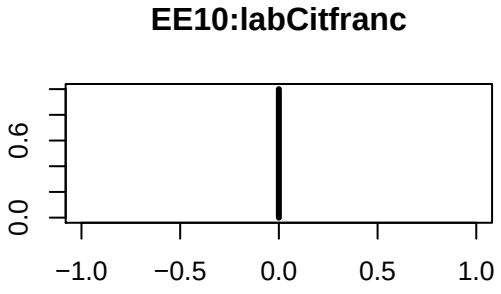
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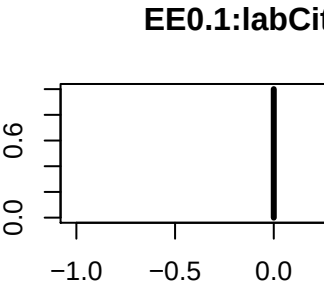
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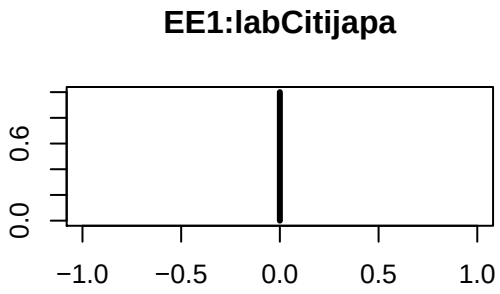
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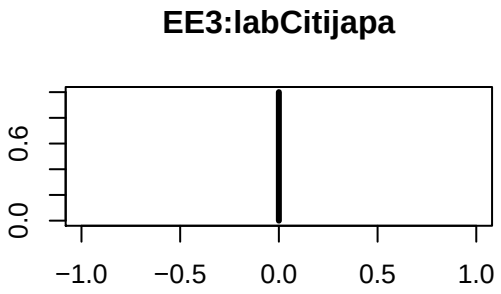
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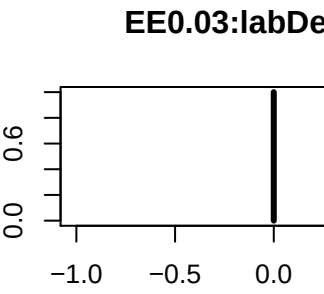
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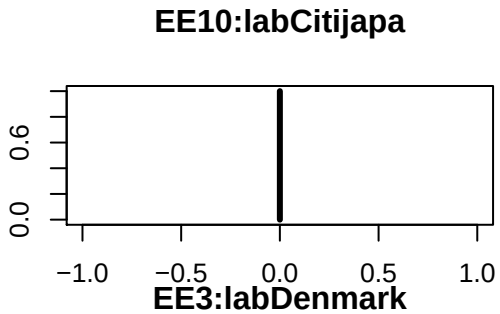
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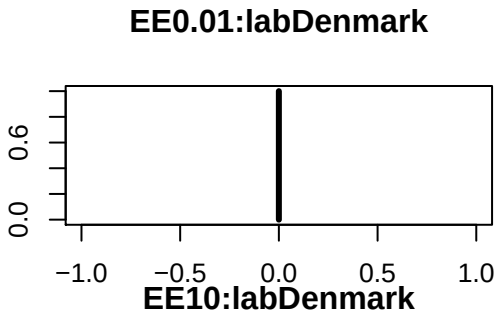
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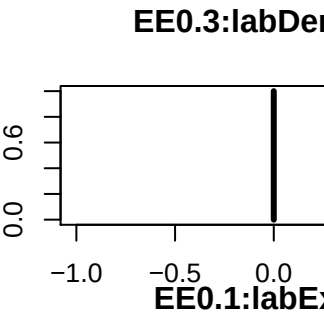
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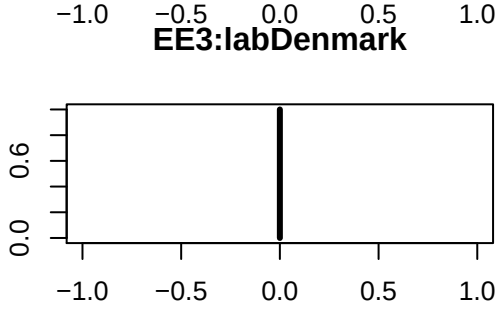
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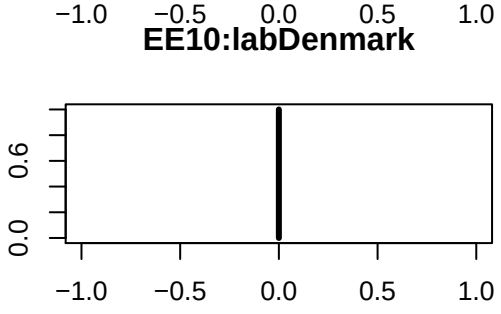
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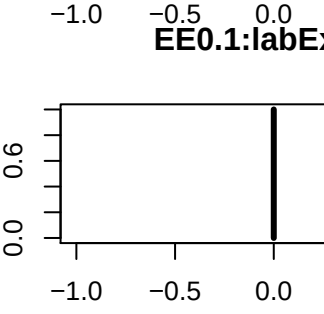
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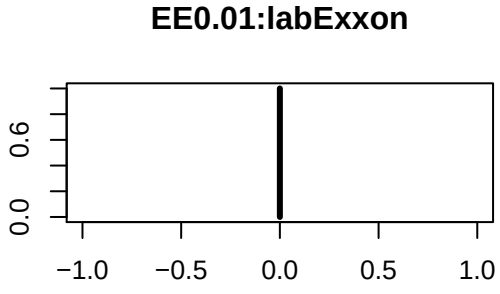
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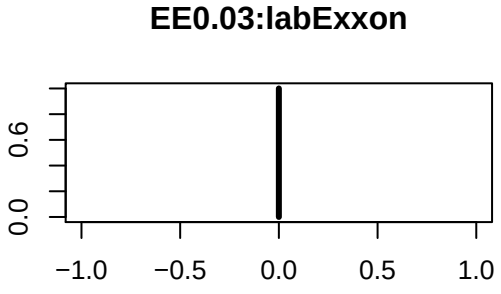
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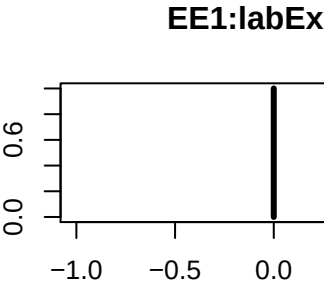
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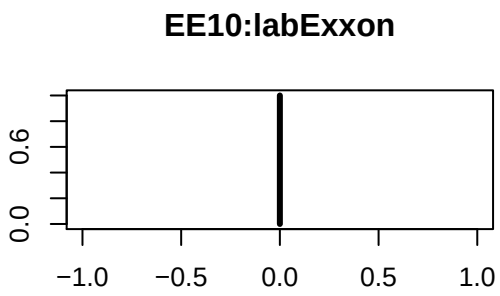
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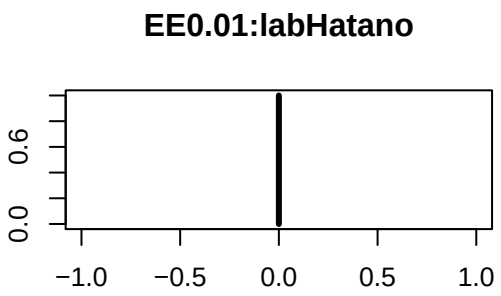
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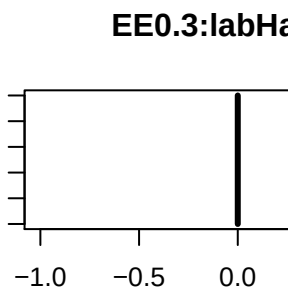
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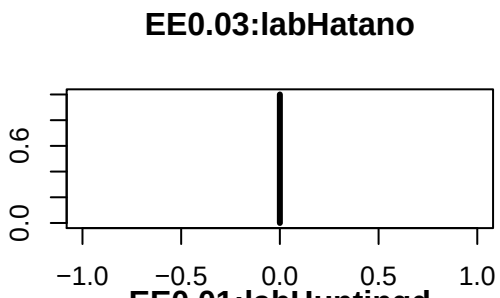
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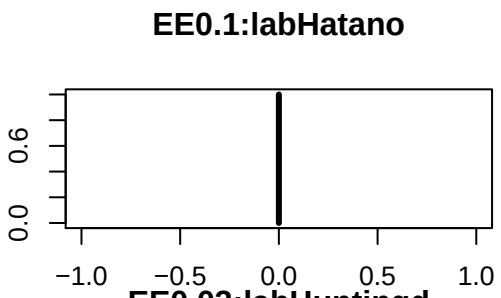
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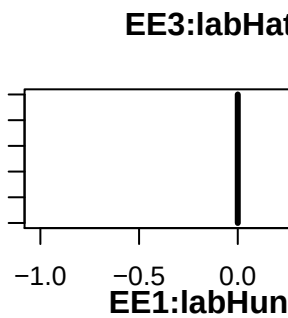
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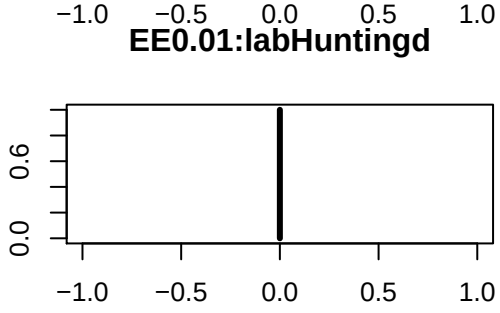
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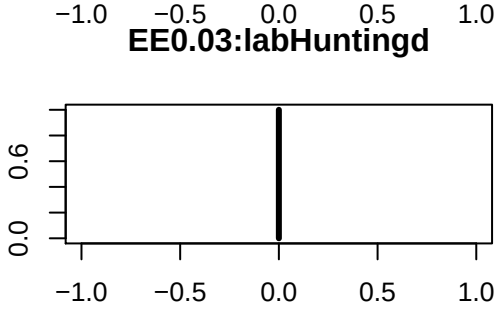
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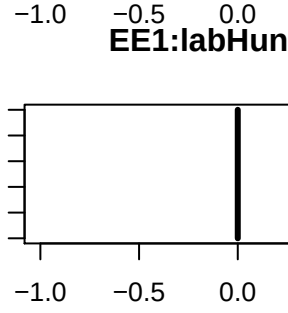
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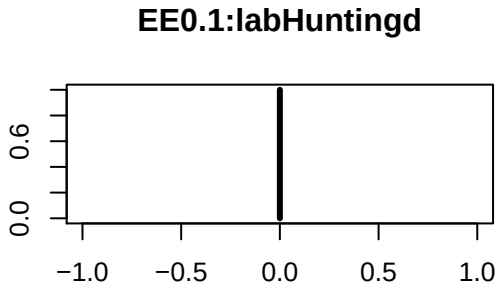
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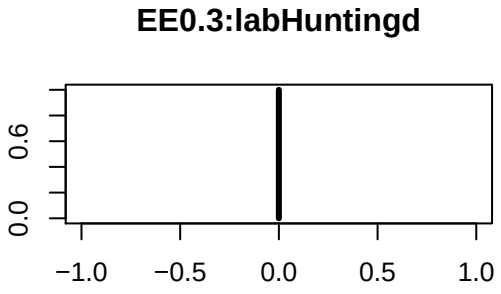
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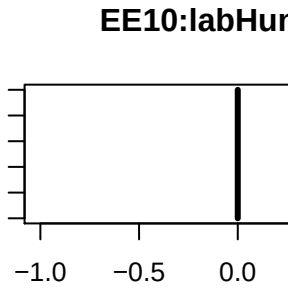
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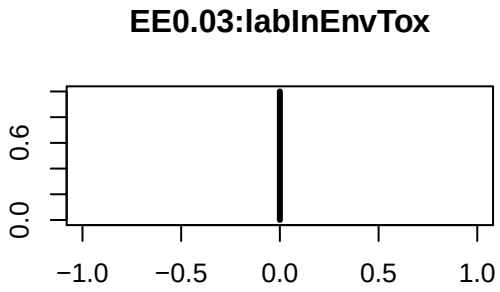
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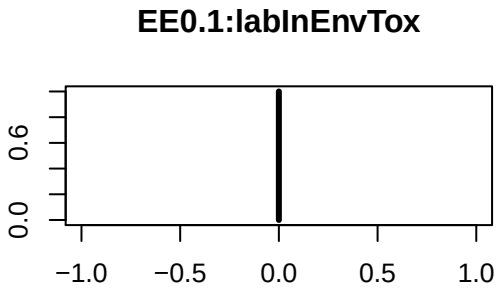
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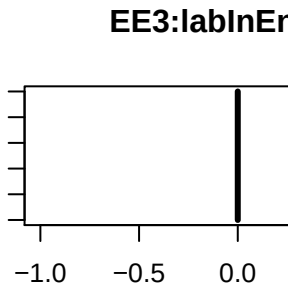
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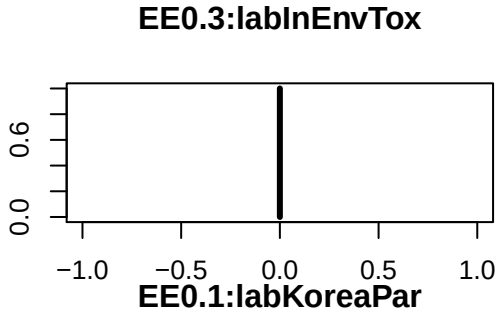
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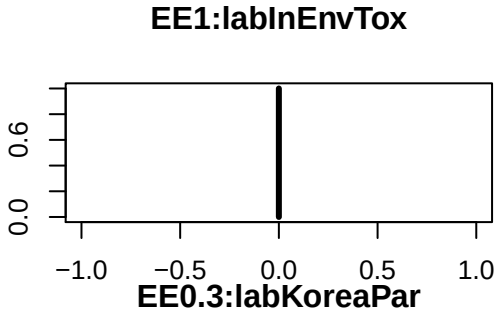
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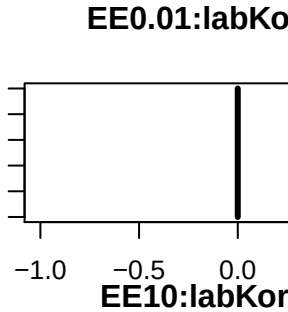
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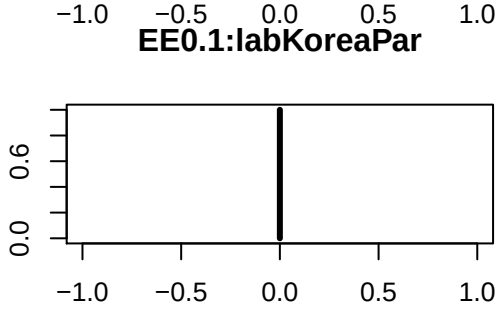
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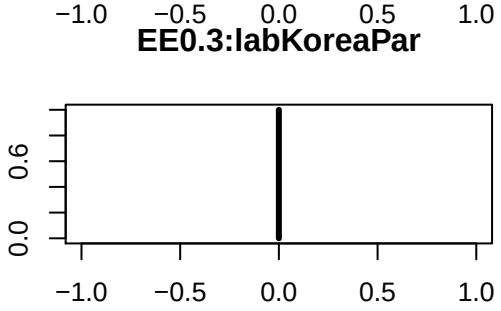
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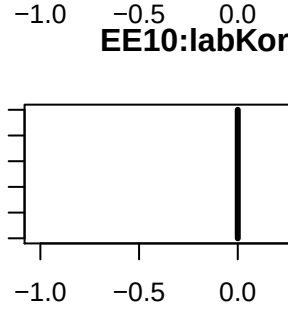
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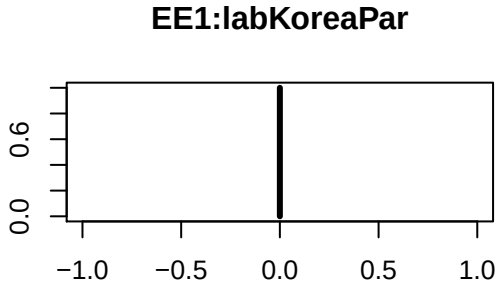
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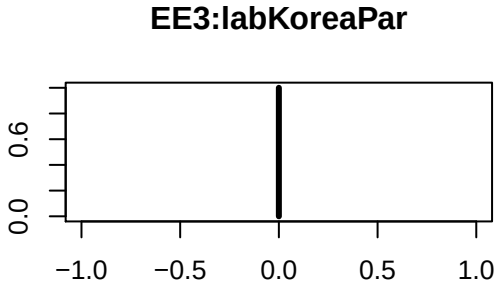
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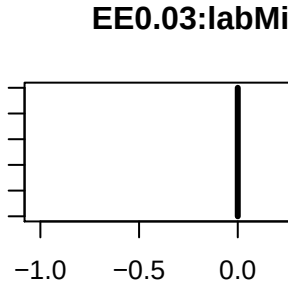
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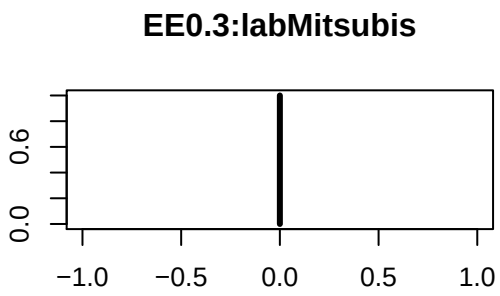
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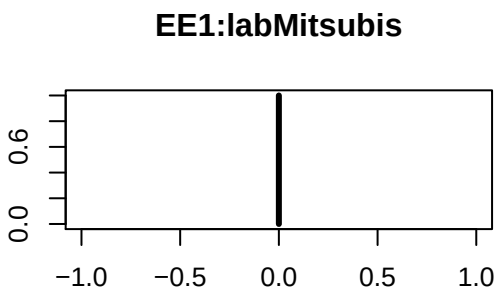
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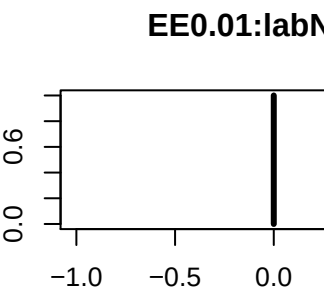
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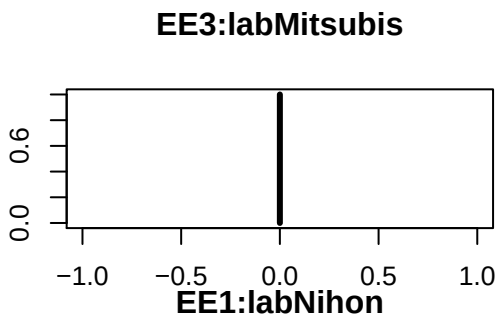
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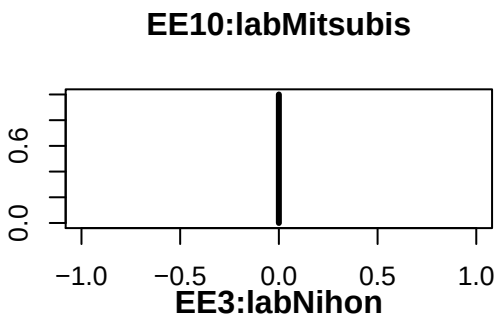
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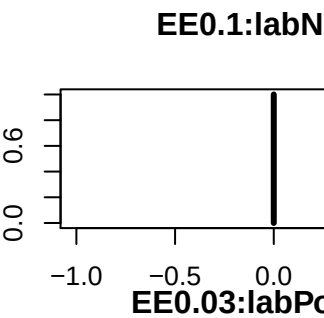
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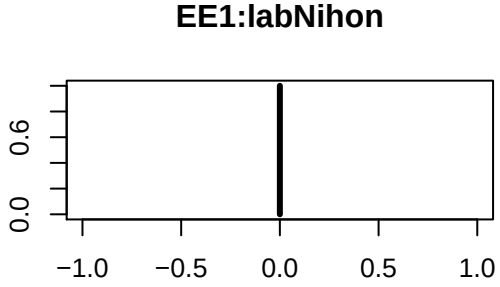
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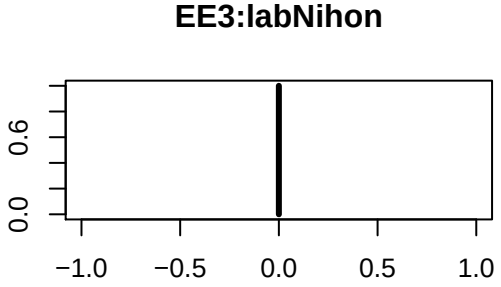
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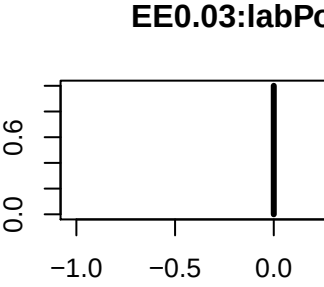
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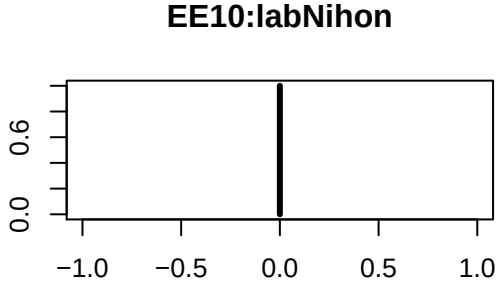
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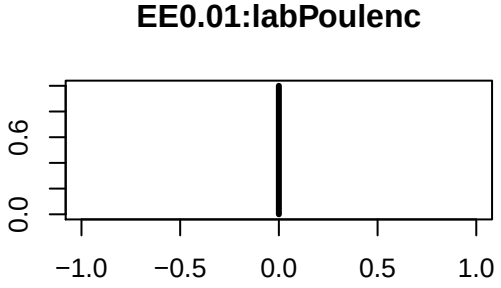
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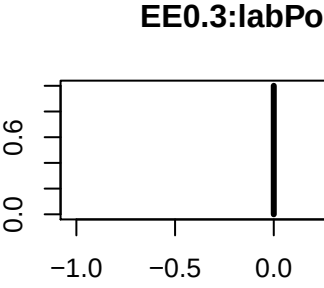
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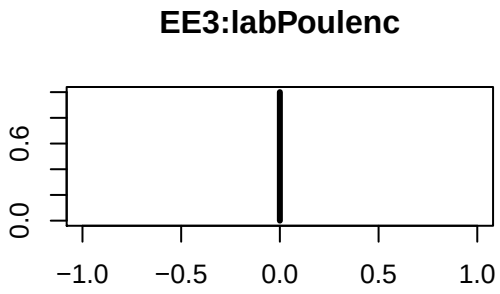
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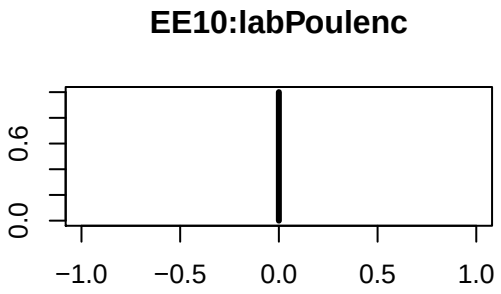
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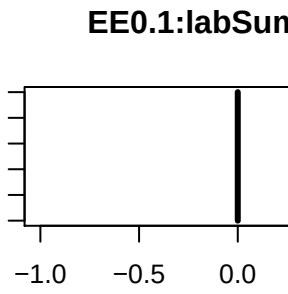
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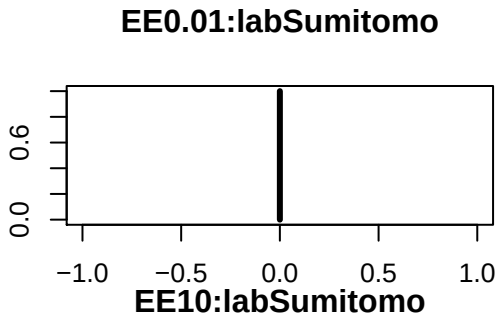
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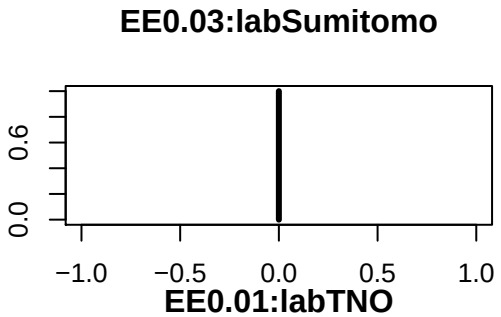
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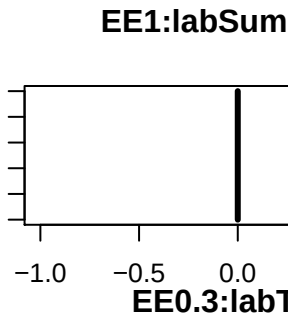
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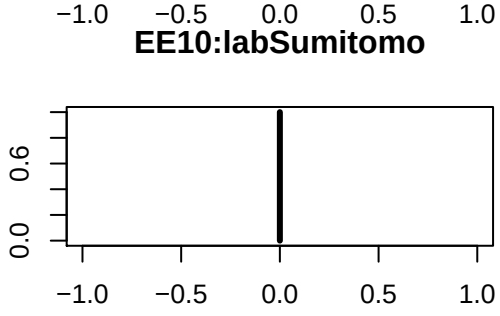
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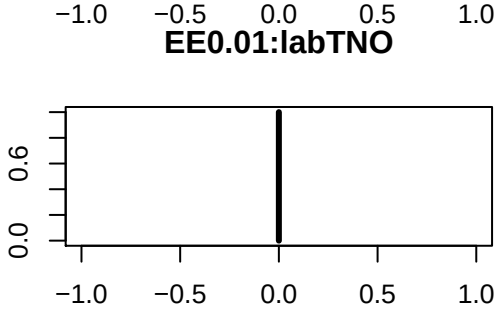
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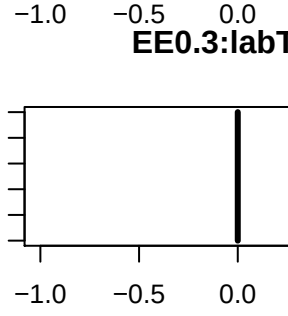
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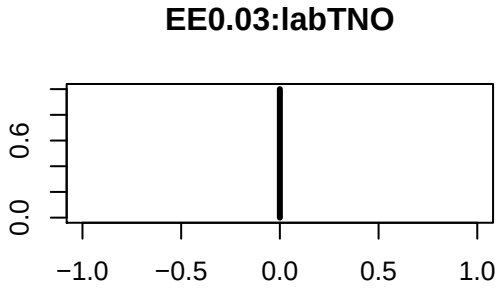
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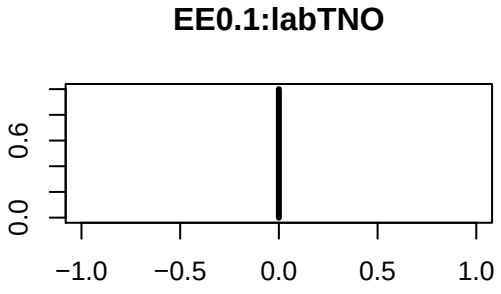
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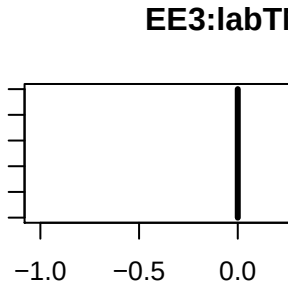
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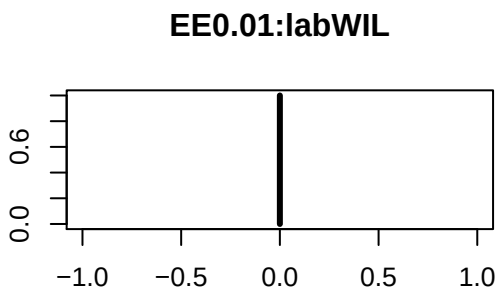
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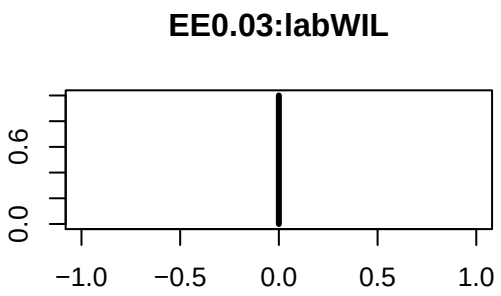
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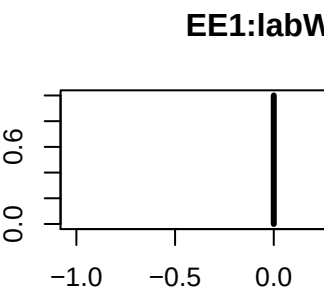
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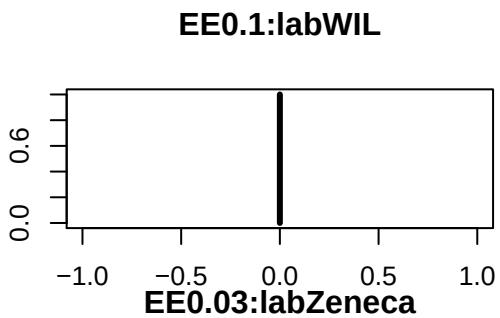
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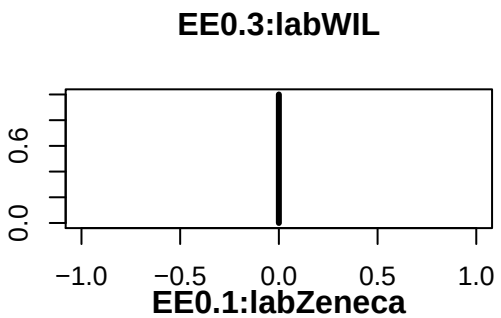
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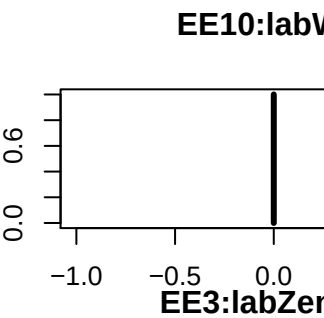
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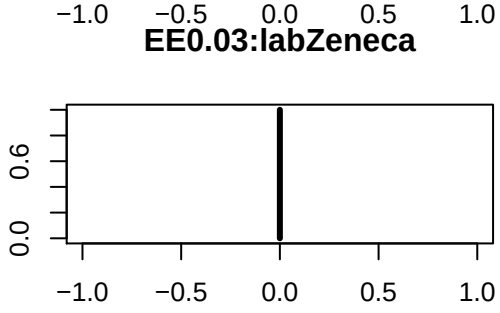
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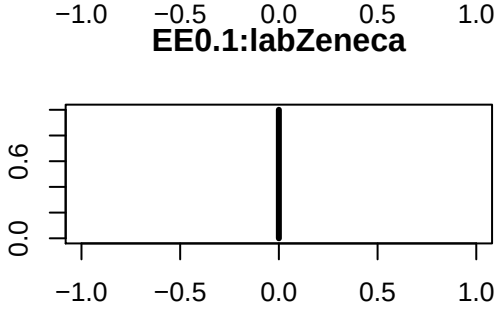
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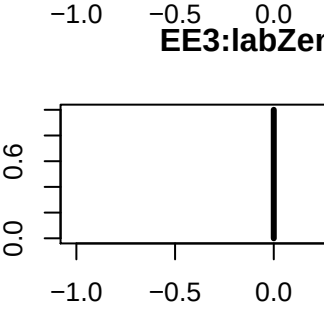
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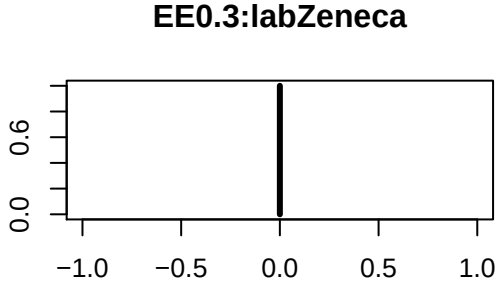
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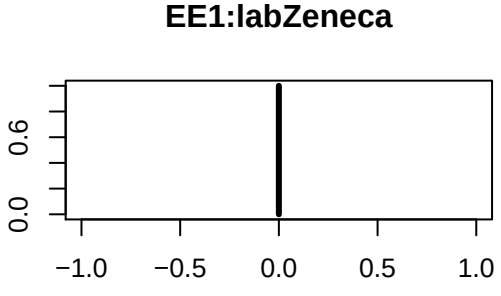
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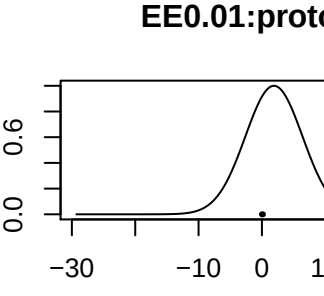
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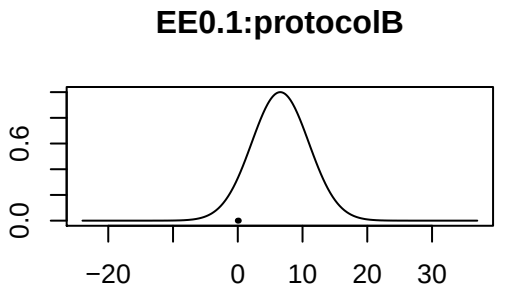
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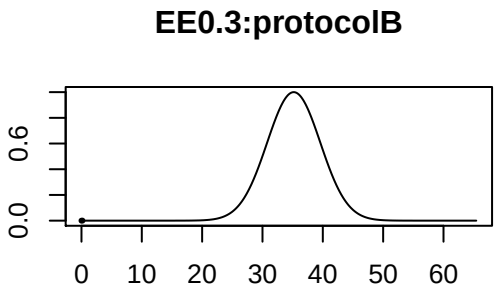
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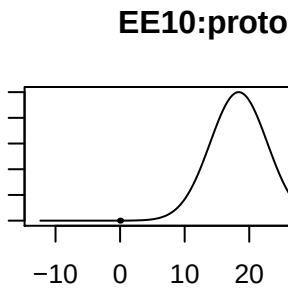
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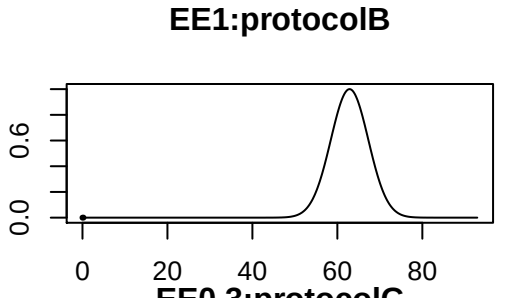
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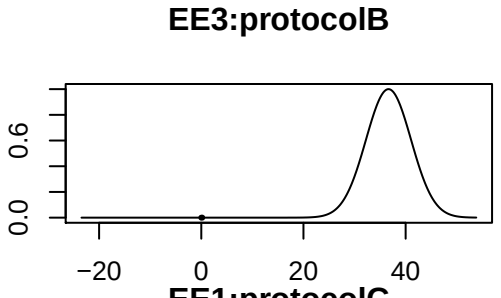
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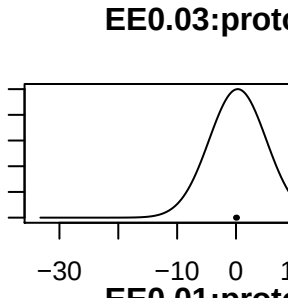
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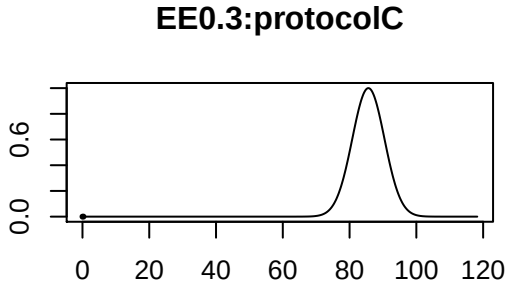
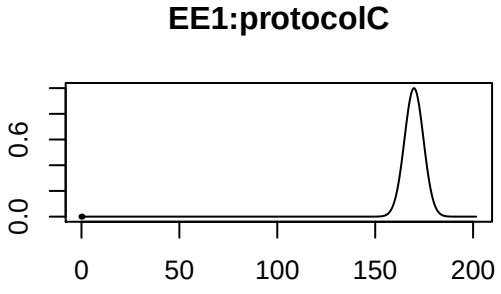
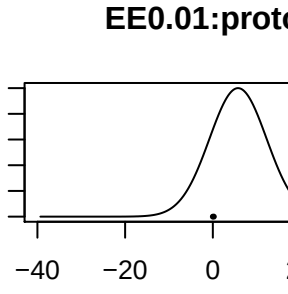
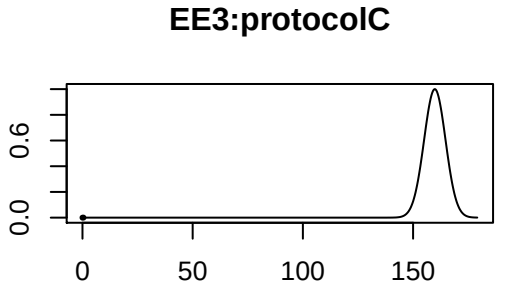
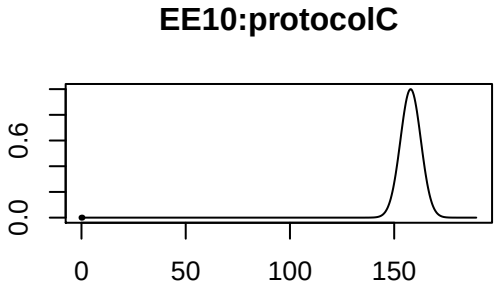
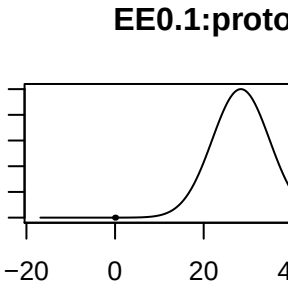

EE0.3:protocolC
0.0
0.6
0
20
40
60
80
100
120

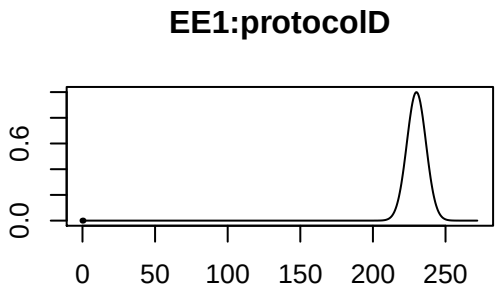

EE1:protocolC
0.0
0.6
0
50
100
150
200

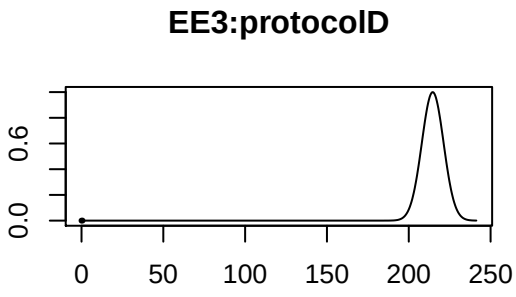

EE0.01:proto
0.0
0.6
−40
−20
0

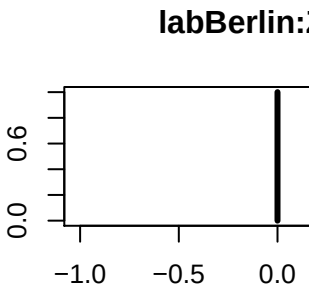

EE3:protocolC
0.0
0.6
0
50
100
150

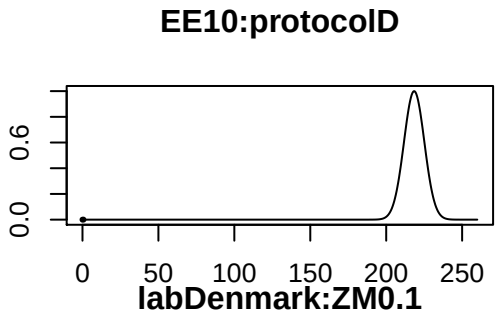

EE10:protocolC
0.0
0.6
0
50
100
150

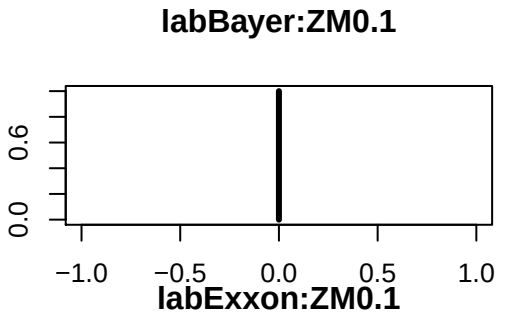

EE0.1:proto
0.0
0.6
−20
0
20

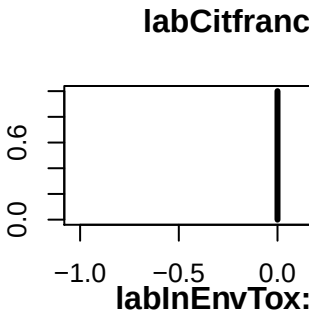

EE1:protocolD
0.0
0.6
0
50
100
150
200
250

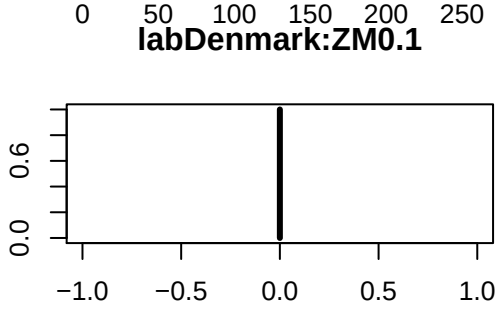

EE3:protocolD
0.0
0.6
0
50
100
150
200
250

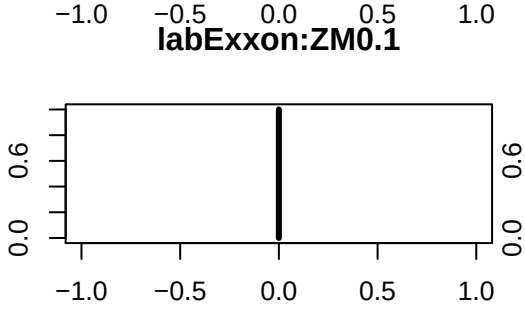

labBerlin:
0.0
0.6
−1.0
−0.5
0.0

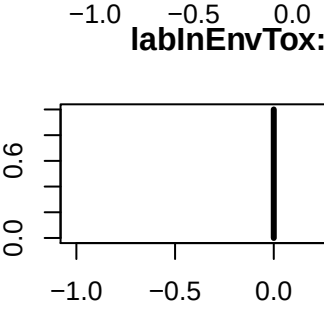

EE10:protocolD
0.0
0.6
0
50
100
150
200
250

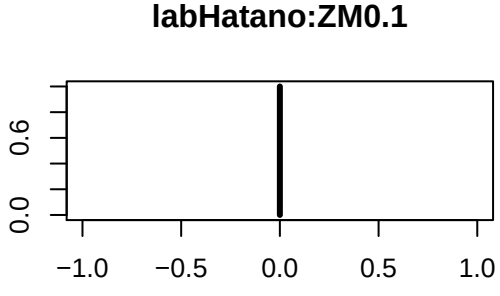

labBayer:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

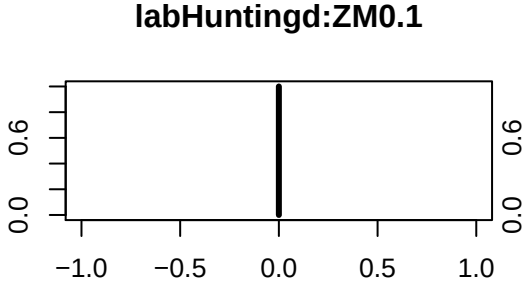

labCitfranc
0.0
0.6
−1.0
−0.5
0.0

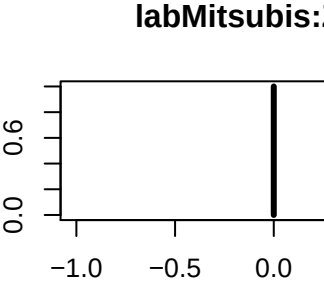

labDenmark:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

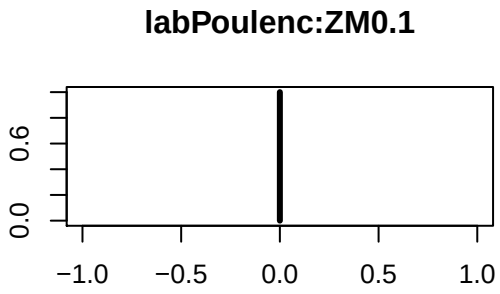

labExxon:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

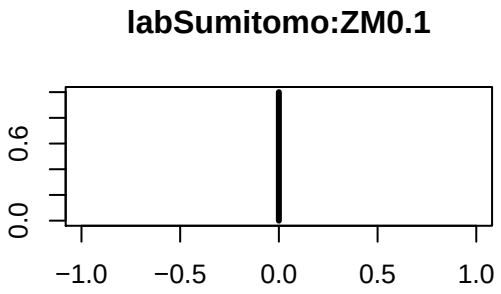

labInEnvTox:
0.0
0.6
−1.0
−0.5
0.0

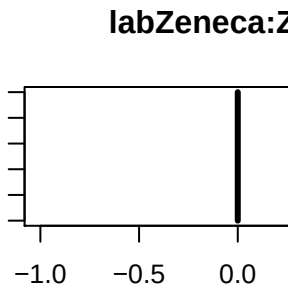

labHatano:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

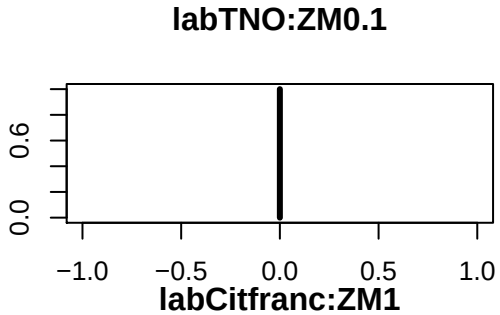

labHuntingd:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

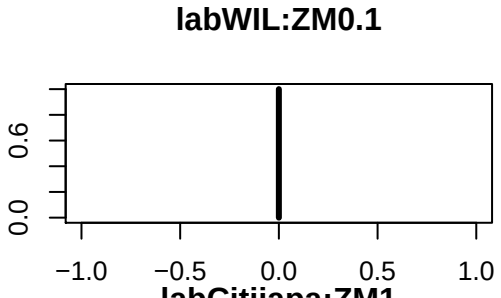

labMitsubis:
0.0
0.6
−1.0
−0.5
0.0

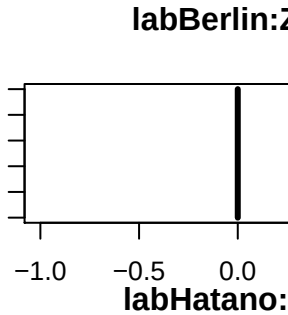

labPoulenc:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

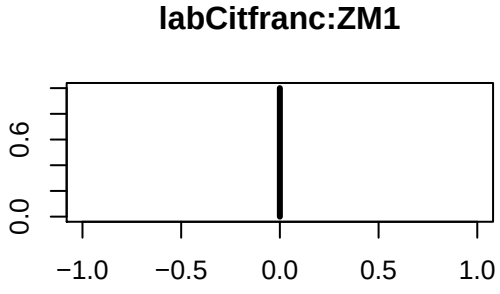

labSumitomo:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

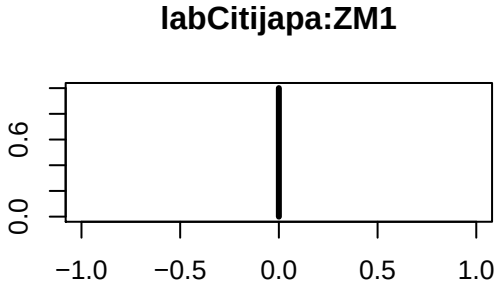

labZeneca:Z
0.0
0.6
−1.0
−0.5
0.0

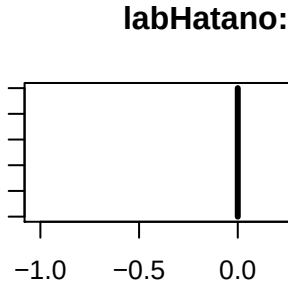

labTNO:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

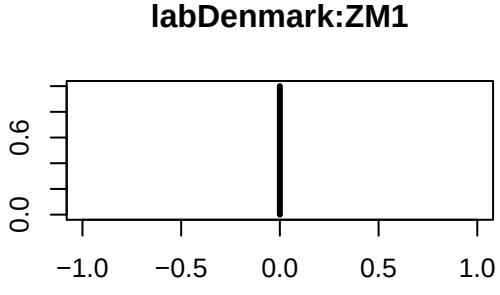

labWIL:ZM0.1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

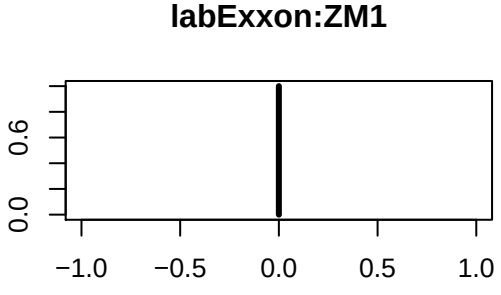

labBerlin:Z
0.0
0.6
−1.0
−0.5
0.0

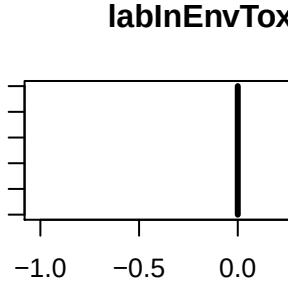

labCitfranc:ZM1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0

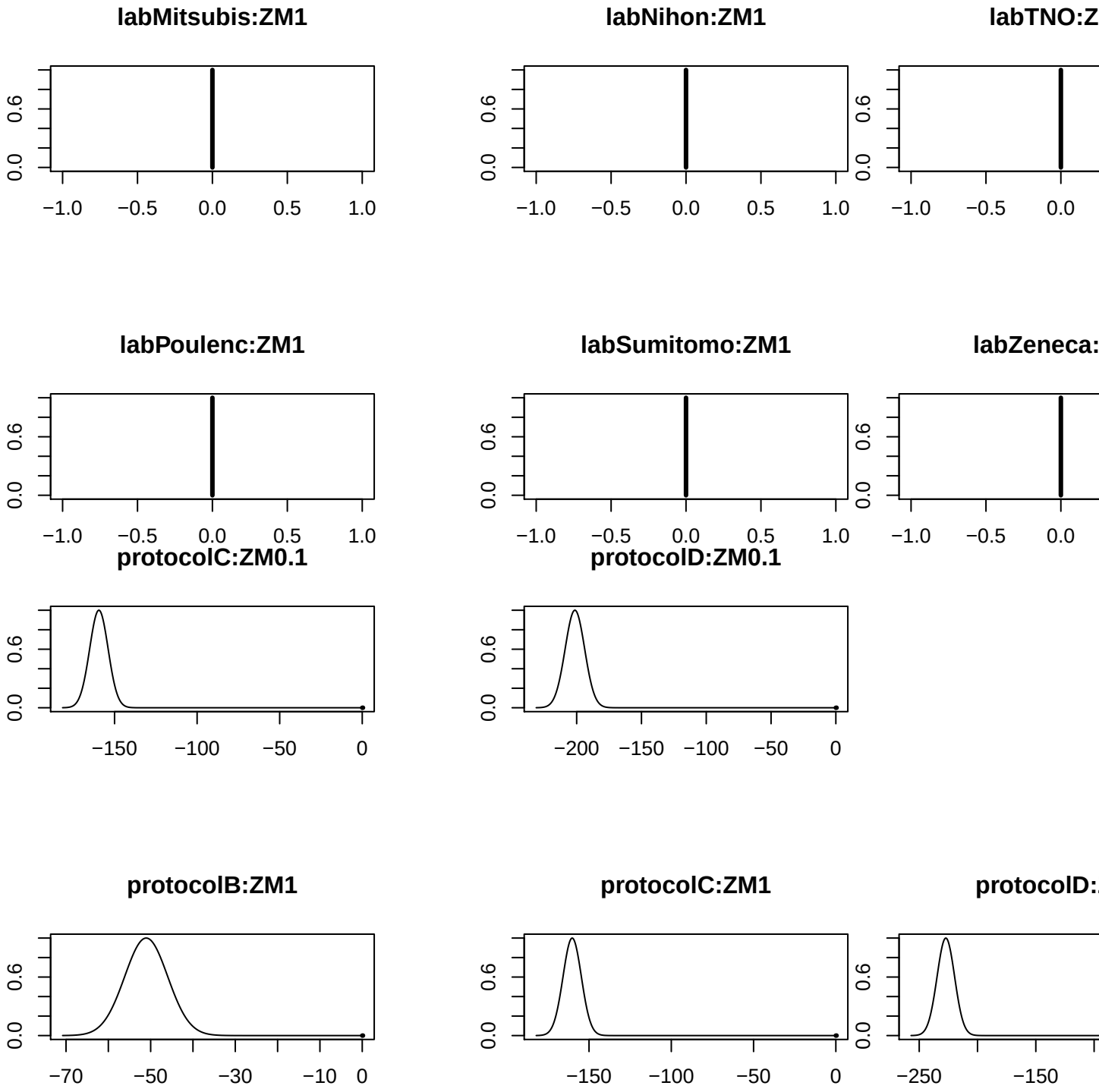

labCitijapa:ZM1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0


labHatano:
0.0
0.6
−1.0
−0.5
0.0


labDenmark:ZM1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0


labExxon:ZM1
0.0
0.6
−1.0
−0.5
0.0
0.5
1.0


labInEnvTox
0.0
0.6
−1.0
−0.5
0.0



b.

Does the dose response vary across labs? If so, are there certain labs that stand out as being different?

See figures in a.

c.

Do the protocols differ in their sensitivity to detecting estrogenic and anti-estrogenic effects? If so, is there one protocol that can be recommended?

```
confint(coef(bas1))
```

```
##                           2.5%        97.5%          beta
## Intercept            99.9634854  101.7486490  100.82851700
## EE0.01               -7.0899102    5.0961915   -1.18653174
## EE0.03               -6.3461745    5.5339375   -0.59179098
## EE0.1                -3.8796458    7.7245088    1.72987554
## EE0.3                 0.3270019   11.9424794    5.94190996
## EE1                  23.9758790   35.5834545   29.58700766
## EE3                  65.5977553   77.2026835   71.63907237
## EE10                 85.7773087   97.3814196   91.82098640
## labBayer              4.2265969   21.7968569   12.90273900
## labBerlin            14.8207481   31.7939841   23.63907831
## labChungKor          26.7229829   41.4198436   34.24246334
## labCitfranc          15.3480654   31.8894843   23.96033309
## labCitijapa          14.6792670   28.7011993   21.77222388
## labDenmark           11.8219810   29.0851938   20.53175514
## labExxon             14.7209057   31.6646678   23.53503627
## labHatano            15.5268897   29.3054604   22.33364563
## labHuntingd         -49.5120607  -27.2976560  -38.74951798
## labInEnvTox           4.6209741   19.1197913   11.88291481
## labKoreaPar          -5.2710045   10.0851675    2.31774371
## labMitsubis          13.2919192   27.0650258   20.06907414
## labNihon              6.7580996   20.4847438   13.70687247
## labPoulenc           -7.9649679    8.7278134    0.34770812
## labSumitomo          20.4358141   34.4898450   27.68806203
## labTNO               14.6870243   29.6334401   22.11022279
## labWIL                4.5981485   19.3121859   12.15273474
## labZeneca            -2.4314837   12.2201105    4.76057607
## protocolB            -8.6001854    1.9465593   -3.50007354
## protocolC            54.3364385   83.9884834   70.77908012
## protocolD            39.1949594   73.3408090   57.68268776
## ZM0.1               -16.0812550   -2.7880643   -9.64511839
## ZM1                 -62.7020795  -49.3943017  -55.77804887
## weight                0.0000000    0.1301594    0.04618206
## EE0.01:labBayer       0.0000000    0.0000000    0.00000000
## EE0.03:labBayer       0.0000000    0.0000000    0.00000000
## EE0.1:labBayer        0.0000000    0.0000000    0.00000000
## EE0.3:labBayer        0.0000000    0.0000000    0.00000000
## EE1:labBayer          0.0000000    0.0000000    0.00000000
## EE3:labBayer          0.0000000    0.0000000    0.00000000
## EE10:labBayer         0.0000000    0.0000000    0.00000000
## EE0.01:labBerlin      0.0000000    0.0000000    0.00000000
## EE0.03:labBerlin      0.0000000    0.0000000    0.00000000
## EE0.1:labBerlin       0.0000000    0.0000000    0.00000000
## EE0.3:labBerlin       0.0000000    0.0000000    0.00000000
## EE1:labBerlin         0.0000000    0.0000000    0.00000000
## EE3:labBerlin         0.0000000    0.0000000    0.00000000
## EE10:labBerlin        0.0000000    0.0000000    0.00000000
## EE0.01:labChungKor    0.0000000    0.0000000    0.00000000
```

```
## EE0.03:labChungKor    0.0000000    0.0000000    0.00000000
## EE0.1:labChungKor     0.0000000    0.0000000    0.00000000
## EE0.3:labChungKor     0.0000000    0.0000000    0.00000000
## EE1:labChungKor       0.0000000    0.0000000    0.00000000
## EE3:labChungKor       0.0000000    0.0000000    0.00000000
## EE10:labChungKor      0.0000000    0.0000000    0.00000000
## EE0.01:labCitfranc    0.0000000    0.0000000    0.00000000
## EE0.03:labCitfranc    0.0000000    0.0000000    0.00000000
## EE0.1:labCitfranc     0.0000000    0.0000000    0.00000000
## EE0.3:labCitfranc     0.0000000    0.0000000    0.00000000
## EE1:labCitfranc       0.0000000    0.0000000    0.00000000
## EE3:labCitfranc       0.0000000    0.0000000    0.00000000
## EE10:labCitfranc      0.0000000    0.0000000    0.00000000
## EE0.01:labCitijapa    0.0000000    0.0000000    0.00000000
## EE0.03:labCitijapa    0.0000000    0.0000000    0.00000000
## EE0.1:labCitijapa     0.0000000    0.0000000    0.00000000
## EE0.3:labCitijapa     0.0000000    0.0000000    0.00000000
## EE1:labCitijapa       0.0000000    0.0000000    0.00000000
## EE3:labCitijapa       0.0000000    0.0000000    0.00000000
## EE10:labCitijapa      0.0000000    0.0000000    0.00000000
## EE0.01:labDenmark     0.0000000    0.0000000    0.00000000
## EE0.03:labDenmark     0.0000000    0.0000000    0.00000000
## EE0.1:labDenmark      0.0000000    0.0000000    0.00000000
## EE0.3:labDenmark      0.0000000    0.0000000    0.00000000
## EE1:labDenmark        0.0000000    0.0000000    0.00000000
## EE3:labDenmark        0.0000000    0.0000000    0.00000000
## EE10:labDenmark       0.0000000    0.0000000    0.00000000
## EE0.01:labExxon       0.0000000    0.0000000    0.00000000
## EE0.03:labExxon       0.0000000    0.0000000    0.00000000
## EE0.1:labExxon        0.0000000    0.0000000    0.00000000
## EE0.3:labExxon        0.0000000    0.0000000    0.00000000
## EE1:labExxon          0.0000000    0.0000000    0.00000000
## EE3:labExxon          0.0000000    0.0000000    0.00000000
## EE10:labExxon         0.0000000    0.0000000    0.00000000
## EE0.01:labHatano      0.0000000    0.0000000    0.00000000
## EE0.03:labHatano      0.0000000    0.0000000    0.00000000
## EE0.1:labHatano       0.0000000    0.0000000    0.00000000
## EE0.3:labHatano       0.0000000    0.0000000    0.00000000
## EE1:labHatano         0.0000000    0.0000000    0.00000000
## EE3:labHatano         0.0000000    0.0000000    0.00000000
## EE10:labHatano        0.0000000    0.0000000    0.00000000
## EE0.01:labHuntingd    0.0000000    0.0000000    0.00000000
## EE0.03:labHuntingd    0.0000000    0.0000000    0.00000000
## EE0.1:labHuntingd     0.0000000    0.0000000    0.00000000
## EE0.3:labHuntingd     0.0000000    0.0000000    0.00000000
## EE1:labHuntingd       0.0000000    0.0000000    0.00000000
## EE3:labHuntingd       0.0000000    0.0000000    0.00000000
## EE10:labHuntingd      0.0000000    0.0000000    0.00000000
## EE0.01:labInEnvTox    0.0000000    0.0000000    0.00000000
## EE0.03:labInEnvTox    0.0000000    0.0000000    0.00000000
## EE0.1:labInEnvTox     0.0000000    0.0000000    0.00000000
## EE0.3:labInEnvTox     0.0000000    0.0000000    0.00000000
## EE1:labInEnvTox       0.0000000    0.0000000    0.00000000
## EE3:labInEnvTox       0.0000000    0.0000000    0.00000000
```

```
## EE10:labInEnvTox      0.0000000    0.0000000    0.00000000
## EE0.01:labKoreaPar    0.0000000    0.0000000    0.00000000
## EE0.03:labKoreaPar    0.0000000    0.0000000    0.00000000
## EE0.1:labKoreaPar     0.0000000    0.0000000    0.00000000
## EE0.3:labKoreaPar     0.0000000    0.0000000    0.00000000
## EE1:labKoreaPar       0.0000000    0.0000000    0.00000000
## EE3:labKoreaPar       0.0000000    0.0000000    0.00000000
## EE10:labKoreaPar      0.0000000    0.0000000    0.00000000
## EE0.01:labMitsubis    0.0000000    0.0000000    0.00000000
## EE0.03:labMitsubis    0.0000000    0.0000000    0.00000000
## EE0.1:labMitsubis     0.0000000    0.0000000    0.00000000
## EE0.3:labMitsubis     0.0000000    0.0000000    0.00000000
## EE1:labMitsubis       0.0000000    0.0000000    0.00000000
## EE3:labMitsubis       0.0000000    0.0000000    0.00000000
## EE10:labMitsubis      0.0000000    0.0000000    0.00000000
## EE0.01:labNihon       0.0000000    0.0000000    0.00000000
## EE0.03:labNihon       0.0000000    0.0000000    0.00000000
## EE0.1:labNihon        0.0000000    0.0000000    0.00000000
## EE0.3:labNihon        0.0000000    0.0000000    0.00000000
## EE1:labNihon          0.0000000    0.0000000    0.00000000
## EE3:labNihon          0.0000000    0.0000000    0.00000000
## EE10:labNihon         0.0000000    0.0000000    0.00000000
## EE0.01:labPoulenc     0.0000000    0.0000000    0.00000000
## EE0.03:labPoulenc     0.0000000    0.0000000    0.00000000
## EE0.1:labPoulenc      0.0000000    0.0000000    0.00000000
## EE0.3:labPoulenc      0.0000000    0.0000000    0.00000000
## EE1:labPoulenc        0.0000000    0.0000000    0.00000000
## EE3:labPoulenc        0.0000000    0.0000000    0.00000000
## EE10:labPoulenc       0.0000000    0.0000000    0.00000000
## EE0.01:labSumitomo    0.0000000    0.0000000    0.00000000
## EE0.03:labSumitomo    0.0000000    0.0000000    0.00000000
## EE0.1:labSumitomo     0.0000000    0.0000000    0.00000000
## EE0.3:labSumitomo     0.0000000    0.0000000    0.00000000
## EE1:labSumitomo       0.0000000    0.0000000    0.00000000
## EE3:labSumitomo       0.0000000    0.0000000    0.00000000
## EE10:labSumitomo      0.0000000    0.0000000    0.00000000
## EE0.01:labTNO         0.0000000    0.0000000    0.00000000
## EE0.03:labTNO         0.0000000    0.0000000    0.00000000
## EE0.1:labTNO          0.0000000    0.0000000    0.00000000
## EE0.3:labTNO          0.0000000    0.0000000    0.00000000
## EE1:labTNO            0.0000000    0.0000000    0.00000000
## EE3:labTNO            0.0000000    0.0000000    0.00000000
## EE10:labTNO           0.0000000    0.0000000    0.00000000
## EE0.01:labWIL         0.0000000    0.0000000    0.00000000
## EE0.03:labWIL         0.0000000    0.0000000    0.00000000
## EE0.1:labWIL          0.0000000    0.0000000    0.00000000
## EE0.3:labWIL          0.0000000    0.0000000    0.00000000
## EE1:labWIL            0.0000000    0.0000000    0.00000000
## EE3:labWIL            0.0000000    0.0000000    0.00000000
## EE10:labWIL           0.0000000    0.0000000    0.00000000
## EE0.01:labZeneca      0.0000000    0.0000000    0.00000000
## EE0.03:labZeneca      0.0000000    0.0000000    0.00000000
## EE0.1:labZeneca       0.0000000    0.0000000    0.00000000
## EE0.3:labZeneca       0.0000000    0.0000000    0.00000000
```

```
## EE1:labZeneca          0.0000000    0.0000000    0.00000000
## EE3:labZeneca          0.0000000    0.0000000    0.00000000
## EE10:labZeneca         0.0000000    0.0000000    0.00000000
## EE0.01:protocolB      -6.8298775   11.2127205    1.89630560
## EE0.03:protocolB      -6.2774906   11.5567282    2.34409878
## EE0.1:protocolB       -1.9741129   15.6790387    6.55911454
## EE0.3:protocolB       26.6466198   44.2945637   35.17766721
## EE1:protocolB         53.6872517   71.3468552   62.87308783
## EE3:protocolB         28.1080112   45.7478983   36.64803171
## EE10:protocolB         9.1593308   26.8661141   18.36769331
## EE0.01:protocolC      -8.4968402   11.0994709    1.01031579
## EE0.03:protocolC      -9.1114635   10.2959307    0.28941203
## EE0.1:protocolC       -0.3148082   18.9164995    9.68541798
## EE0.3:protocolC       75.6113868   94.8380853   85.63123600
## EE1:protocolC        160.0832794  179.2972867  169.80766748
## EE3:protocolC        149.9611168  169.2482099  159.85569811
## EE10:protocolC       148.3581071  167.7779765  157.89403523
## EE0.01:protocolD      -6.8552173   19.2104120    5.74642392
## EE0.03:protocolD     -11.5420525   14.6548057    2.11132584
## EE0.1:protocolD       15.3595247   41.1041122   28.39008031
## EE0.3:protocolD      123.2493610  149.0722732  136.46645520
## EE1:protocolD        217.1209210  243.2373794  229.96046349
## EE3:protocolD        202.0149067  228.2972836  214.63658437
## EE10:protocolD       204.6610155  231.1203307  218.42965678
## labBayer:ZM0.1         0.0000000    0.0000000    0.00000000
## labBerlin:ZM0.1        0.0000000    0.0000000    0.00000000
## labChungKor:ZM0.1      0.0000000    0.0000000    0.00000000
## labCitfranc:ZM0.1      0.0000000    0.0000000    0.00000000
## labCitijapa:ZM0.1      0.0000000    0.0000000    0.00000000
## labDenmark:ZM0.1       0.0000000    0.0000000    0.00000000
## labExxon:ZM0.1         0.0000000    0.0000000    0.00000000
## labHatano:ZM0.1        0.0000000    0.0000000    0.00000000
## labHuntingd:ZM0.1      0.0000000    0.0000000    0.00000000
## labInEnvTox:ZM0.1      0.0000000    0.0000000    0.00000000
## labKoreaPar:ZM0.1      0.0000000    0.0000000    0.00000000
## labMitsubis:ZM0.1      0.0000000    0.0000000    0.00000000
## labNihon:ZM0.1         0.0000000    0.0000000    0.00000000
## labPoulenc:ZM0.1       0.0000000    0.0000000    0.00000000
## labSumitomo:ZM0.1      0.0000000    0.0000000    0.00000000
## labTNO:ZM0.1           0.0000000    0.0000000    0.00000000
## labWIL:ZM0.1           0.0000000    0.0000000    0.00000000
## labZeneca:ZM0.1        0.0000000    0.0000000    0.00000000
## labBayer:ZM1           0.0000000    0.0000000    0.00000000
## labBerlin:ZM1          0.0000000    0.0000000    0.00000000
## labChungKor:ZM1        0.0000000    0.0000000    0.00000000
## labCitfranc:ZM1        0.0000000    0.0000000    0.00000000
## labCitijapa:ZM1        0.0000000    0.0000000    0.00000000
## labDenmark:ZM1         0.0000000    0.0000000    0.00000000
## labExxon:ZM1           0.0000000    0.0000000    0.00000000
## labHatano:ZM1          0.0000000    0.0000000    0.00000000
## labHuntingd:ZM1        0.0000000    0.0000000    0.00000000
## labInEnvTox:ZM1        0.0000000    0.0000000    0.00000000
## labKoreaPar:ZM1        0.0000000    0.0000000    0.00000000
## labMitsubis:ZM1        0.0000000    0.0000000    0.00000000
```

```
## labNihon:ZM1          0.0000000    0.0000000    0.00000000
## labPoulenc:ZM1        0.0000000    0.0000000    0.00000000
## labSumitomo:ZM1       0.0000000    0.0000000    0.00000000
## labTNO:ZM1            0.0000000    0.0000000    0.00000000
## labWIL:ZM1            0.0000000    0.0000000    0.00000000
## labZeneca:ZM1         0.0000000    0.0000000    0.00000000
## protocolB:ZM0.1     -70.7834959  -50.4822149  -60.94975534
## protocolC:ZM0.1    -170.5569762 -148.3006501 -159.48332372
## protocolD:ZM0.1    -216.7123817 -186.6814970 -201.36040286
## protocolB:ZM1       -60.8828434  -40.5809578  -51.05086720
## protocolC:ZM1      -171.3012343 -149.1127288 -160.23005583
## protocolD:ZM1      -242.4823897 -212.4619059 -227.16534815
## attr(,"Probability")
## [1] 0.95
## attr(,"class")
## [1] "confint.bas"
```

Model Part III

```
## X matrix and scale
X0 = model.matrix(lm.full)[,-1]
X.scaled = scale(X0)/sqrt(n-1)

## data for jags
data = list(Y = bioassay$uterus, X = X.scaled, p = p, n = n)
data$scales =  attr(X.scaled, "scaled:scale")*sqrt(n-1) + 0.00001
data$Xbar = attr(X.scaled, "scaled:center")

## JAGS
rr.model = function() {
  a <- 2
  shape<-a/2

  for (i in 1:n) {
    mu[i] <- alpha0 + inprod(X[i,], alpha)
    Y[i] ~ dnorm(0, phi)
  }
  phi ~ dgamma(1.0E-6, 1.0E-6)  ##jags do not allow improper prior
  alpha0 ~ dnorm(0, 1.0E-6)

  for (j in 1:p) {
    phi.l[j] <- pow(i.phi.l[j], -2)
    prec.beta[j] <- lambda.l[j]*phi*phi.l[j]
    alpha[j] ~ dnorm(0, prec.beta[j])
    # transform back to original coefficients
    beta[j] <- alpha[j]/scales[j]
    lambda.l[j] ~ dgamma(shape, shape)
    i.phi.l[j] ~ dt(0,1,1)%_%T(0,)
  }

  # transform intercept to usual parameterization
  beta0 <- alpha0 - inprod(beta[1:p], Xbar)
```

```
  sigma <- pow(phi, -.5)
}

## parameters to monitor
parameters = c("beta0", "beta", "sigma","lambda.l", "phi.l")

## run jags
jags.result = jags(data, inits=NULL, par=parameters,
                   model=rr.model, n.iter=30000)
```

```
## module glm loaded
```

```
## Compiling model graph
##    Resolving undeclared variables
##    Allocating nodes
## Graph information:
##    Observed stochastic nodes: 2677
##    Unobserved stochastic nodes: 662
##    Total graph size: 601326
##
## Initializing model
```

```
saveRDS(jags.result, "jags.result.rds")
jags.result=readRDS("jags.result.rds")
```

a.

Is the uterotrophic bioassay successful overall at identifying estrogenic effects of EE and anti- estrogenic effects of ZM? Do some labs fail to detect such effects? At what dose level of EE is there a change relative to the control and does this level vary across labs?

```
jags.mcmc = as.mcmc(jags.result$BUGSoutput$sims.matrix)
```

b.

Does the dose response vary across labs? If so, are there certain labs that stand out as being different?

See figures in a.

c.

Do the protocols differ in their sensitivity to detecting estrogenic and anti-estrogenic effects? If so, is there one protocol that can be recommended?