Friday, Mar 24

This in-class demonstration will feature the estimation of Poisson and logistic regression models, and the interpretation of rate and odds ratios.

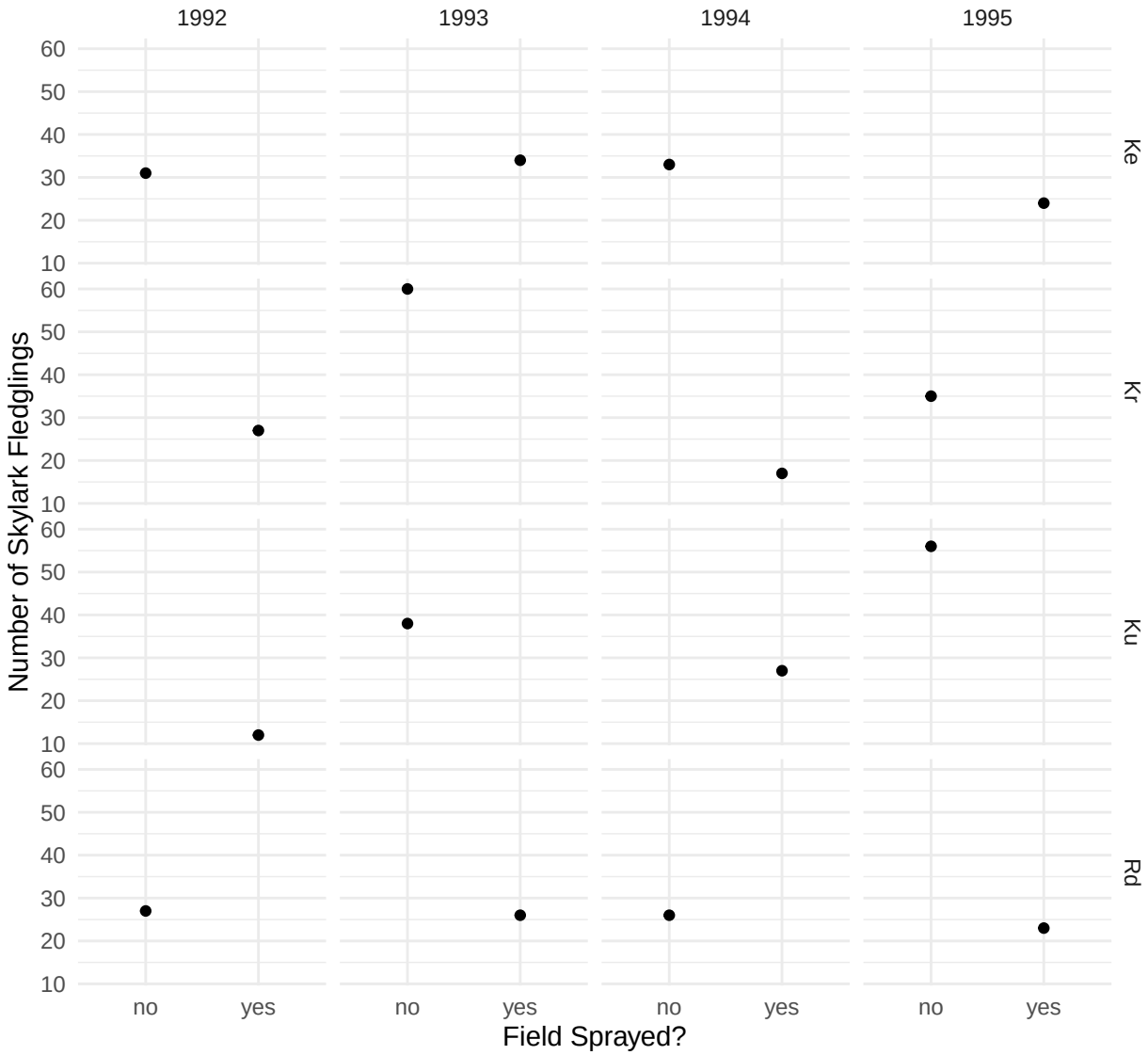
Impact of Pesticides on Skylark Reproductivity

During the four summers from 1992 to 1995 researchers from the National Environmental Research Institute in the Ministry of Environment and Energy in Denmark conducted a study to examine how pesticide use impacts skylark reproduction in barley fields.[1] The study used a fractional factorial design in which each year two of four fields were sprayed with pesticides while the other two fields were not.[2] Which fields were sprayed was alternated so that a field was sprayed every other year. The number of fledgling skylarks produced in each field each year was recorded. The data are in the `skylark` data frame from the **trtools** package. The data are plotted below.

```
library(trtools)
library(ggplot2)
p <- ggplot(skylark, aes(x = spray, y = count)) +
   geom_point() + facet_grid(field ~ year) +
   labs(shape = "Field", x = "Field Sprayed?",
    y = "Number of Skylark Fledglings") + theme_minimal()
plot(p)
```

[1] Odderskær, P., Prang, A., Eknegaard, N., & Andersen, P. N. (1997). Skylark reproduction in pesticide treated fields (Comparative studies of Alauda arvensis breeding performance in sprayed and unsprayed barley fields). *Bekæmpelsesmiddelforskning fra Miljøstyrelsennr*, 32, National Environmental Research Institute, Ministry of the Environment and Energy, Denmark: Danish Environmental Protection Agency.

[2] A fractional factorial design is a design in which observations are made at only a subset of the possible combinations of levels of two or more factors. Such designs are quite economical but can preclude the estimation of interactions. This does not mean that such interactions are not present, but rather that if they are they are confounded with the main effects. For this particular design it is only possible to fully estimate a model with "main effects" for each of the three factors. Ideally factional factorial designs are used when interactions are negligible.



The plot clearly shows the incomplete nature of the fractional factorial design. In any given year, a field either was or was not sprayed. The objective is to investigate the effect of spraying on the number of skylarks while controlling for the effects of year and field.

1. Estimate a Poisson regression model for the number of skylark fledglings as your response variable that will reproduce the following results.

```
cbind(summary(m)$coefficients, confint(m))
```

```
             Estimate Std. Error  z value   Pr(>|z|)    2.5 %   97.5 %
(Intercept)  3.430943    0.13262 25.86999 1.450e-147  3.16352  3.68367
sprayyes    -0.456126    0.09385 -4.86011  1.173e-06 -0.64141 -0.27324
fieldKr      0.049089    0.12672  0.38738  6.985e-01 -0.19929  0.29806
fieldKu      0.004964    0.12800  0.03879  9.691e-01 -0.24611  0.25625
fieldRd     -0.179048    0.13417 -1.33452  1.820e-01 -0.44342  0.08326
year1993     0.462623    0.13064  3.54108  3.985e-04  0.20868  0.72149
year1994     0.060018    0.14149  0.42420  6.714e-01 -0.21735  0.33816
year1995     0.327281    0.13411  2.44041  1.467e-02  0.06596  0.59240
```

Note that here `m` is a model object created using the `glm` function.

Solution: The results can be replicated as follows. Note that the output above indicates that only the "main effects" of spray, field, and year were specified. We can see that there are indicator variables for spray, field, and year, but no interaction terms.

```
m <- glm(count ~ spray + field + year, family = poisson, data = skylark)
cbind(summary(m)$coefficients, confint(m))
```

```
             Estimate Std. Error  z value   Pr(>|z|)    2.5 %   97.5 %
(Intercept)  3.430943    0.13262 25.86999 1.450e-147  3.16352  3.68367
sprayyes    -0.456126    0.09385 -4.86011  1.173e-06 -0.64141 -0.27324
fieldKr      0.049089    0.12672  0.38738  6.985e-01 -0.19929  0.29806
fieldKu      0.004964    0.12800  0.03879  9.691e-01 -0.24611  0.25625
fieldRd     -0.179048    0.13417 -1.33452  1.820e-01 -0.44342  0.08326
year1993     0.462623    0.13064  3.54108  3.985e-04  0.20868  0.72149
year1994     0.060018    0.14149  0.42420  6.714e-01 -0.21735  0.33816
year1995     0.327281    0.13411  2.44041  1.467e-02  0.06596  0.59240
```

2. What is the estimated rate ratio for the effect of spraying? How can this be interpreted?

Solution: We can estimate this rate ratio several ways. Note that since there is no interaction involving spray the field and year does not matter.

```
trtools::contrast(m, tf = exp,
  a = list(spray = "yes", field = "Ke", year = "1992"),
  b = list(spray = "no", field = "Ke", year = "1992"))
```

```
 estimate  lower  upper
   0.6337 0.5273 0.7617
```

```
library(emmeans)
pairs(emmeans(m, ~spray|field*year, type = "response"), infer = TRUE)
```

```
field = Ke, year = 1992:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Kr, year = 1992:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Ku, year = 1992:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Rd, year = 1992:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Ke, year = 1993:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Kr, year = 1993:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Ku, year = 1993:
```

```
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Rd, year = 1993:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Ke, year = 1994:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Kr, year = 1994:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Ku, year = 1994:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Rd, year = 1994:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Ke, year = 1995:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Kr, year = 1995:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Ku, year = 1995:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

field = Rd, year = 1995:
 contrast ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 no / yes  1.58 0.148 Inf      1.31       1.9    1   4.860  <.0001

Confidence level used: 0.95
Intervals are back-transformed from the log scale
Tests are performed on the log scale
```

```
pairs(emmeans(m, ~spray, type = "response"), reverse = TRUE, infer = TRUE)
```

```
 contrast ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 yes / no 0.634 0.0595 Inf     0.527     0.762    1  -4.860  <.0001

Results are averaged over the levels of: field, year
Confidence level used: 0.95
Intervals are back-transformed from the log scale
Tests are performed on the log scale
```

```
exp(cbind(coef(m), confint(m)))
```

```
                     2.5 %  97.5 %
(Intercept) 30.9058 23.6537 39.7921
sprayyes     0.6337  0.5265  0.7609
fieldKr      1.0503  0.8193  1.3472
fieldKu      1.0050  0.7818  1.2921
fieldRd      0.8361  0.6418  1.0868
year1993     1.5882  1.2321  2.0575
year1994     1.0619  0.8046  1.4024
year1995     1.3872  1.0682  1.8083
```

3. What is the estimated expected number of fledglings for each condition?

   Solution: We can estimate this a couple of ways.

```
trtools::contrast(m, tf = exp,
  a = list(spray = c("no", "yes"), field = "Ke", year = "1992"),
  cnames = c("no spray", "spray"))
```

```
         estimate lower upper
no spray    30.91 23.83 40.08
spray       19.59 15.07 25.45
```

```
emmeans(m, ~spray|field*year, type = "response")
```

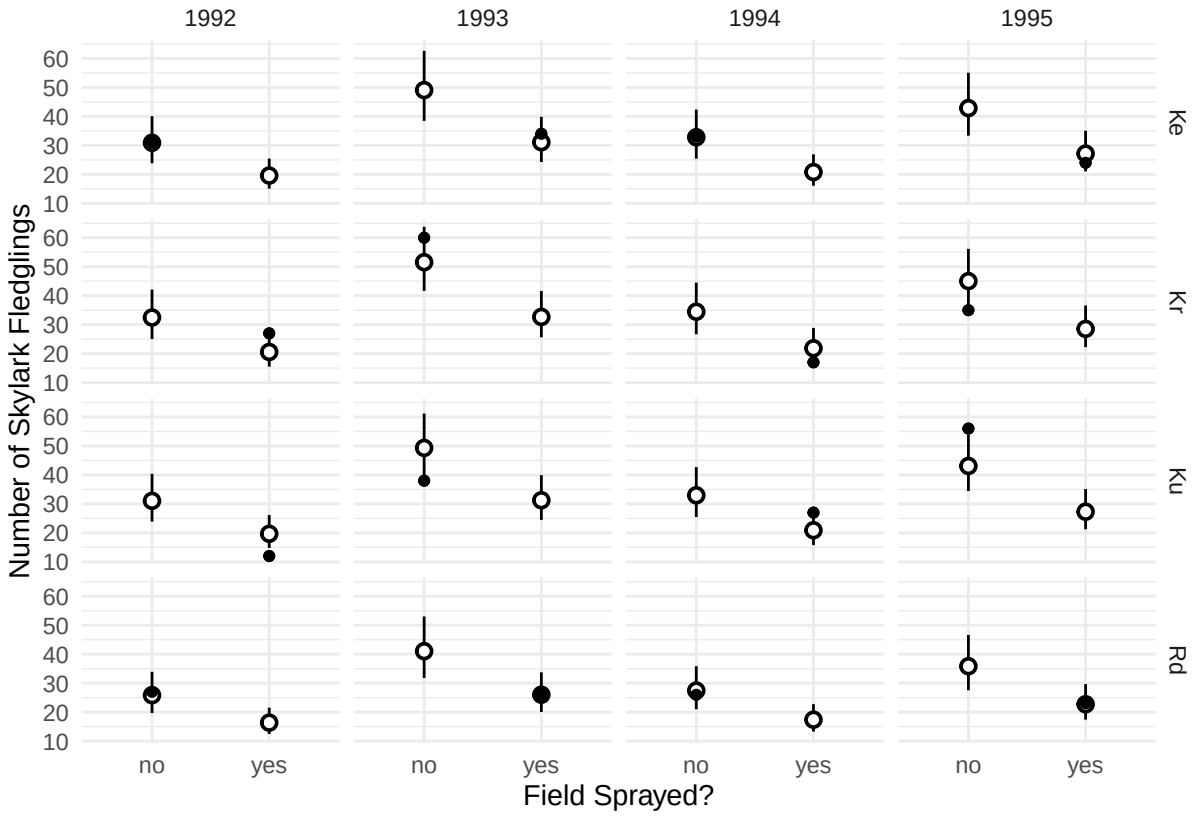
```
field = Ke, year = 1992:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    30.9 4.10 Inf      23.8      40.1
 yes   19.6 2.62 Inf      15.1      25.4

field = Kr, year = 1992:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    32.5 4.31 Inf      25.0      42.1
 yes   20.6 2.97 Inf      15.5      27.3

field = Ku, year = 1992:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    31.1 4.16 Inf      23.9      40.4
 yes   19.7 2.87 Inf      14.8      26.2

field = Rd, year = 1992:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    25.8 3.58 Inf      19.7      33.9
 yes   16.4 2.28 Inf      12.5      21.5

field = Ke, year = 1993:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    49.1 6.11 Inf      38.5      62.6
 yes   31.1 3.94 Inf      24.3      39.9

field = Kr, year = 1993:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    51.6 5.59 Inf      41.7      63.8
 yes   32.7 4.04 Inf      25.6      41.6
```

```
field = Ku, year = 1993:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    49.3 5.42 Inf      39.8      61.2
 yes   31.3 3.90 Inf      24.5      39.9

field = Rd, year = 1993:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    41.0 5.37 Inf      31.8      53.0
 yes   26.0 3.45 Inf      20.1      33.7

field = Ke, year = 1994:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    32.8 4.28 Inf      25.4      42.4
 yes   20.8 2.73 Inf      16.1      26.9

field = Kr, year = 1994:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    34.5 4.50 Inf      26.7      44.5
 yes   21.8 3.11 Inf      16.5      28.9

field = Ku, year = 1994:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    33.0 4.34 Inf      25.5      42.7
 yes   20.9 3.00 Inf      15.8      27.7

field = Rd, year = 1994:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    27.4 3.74 Inf      21.0      35.8
 yes   17.4 2.39 Inf      13.3      22.8

field = Ke, year = 1995:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    42.9 5.49 Inf      33.4      55.1
 yes   27.2 3.54 Inf      21.1      35.1

field = Kr, year = 1995:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    45.0 5.07 Inf      36.1      56.1
 yes   28.5 3.63 Inf      22.2      36.6

field = Ku, year = 1995:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    43.1 4.91 Inf      34.5      53.9
 yes   27.3 3.51 Inf      21.2      35.1

field = Rd, year = 1995:
 spray rate   SE  df asymp.LCL asymp.UCL
 no    35.8 4.81 Inf      27.6      46.6
 yes   22.7 3.09 Inf      17.4      29.7

Confidence level used: 0.95
Intervals are back-transformed from the log scale
```

```
d <- expand.grid(spray = c("yes", "no"), field = c("Ke","Kr","Ku","Rd"),
  year = c("1992","1993","1994","1995"))
cbind(d, trtools::glmint(m, newdata = d))
```

```
   spray field year   fit   low   upp
1    yes    Ke 1992 19.59 15.07 25.45
2     no    Ke 1992 30.91 23.83 40.08
3    yes    Kr 1992 20.57 15.50 27.31
4     no    Kr 1992 32.46 25.02 42.11
5    yes    Ku 1992 19.68 14.80 26.18
6     no    Ku 1992 31.06 23.88 40.39
7    yes    Rd 1992 16.38 12.46 21.52
8     no    Rd 1992 25.84 19.69 33.90
9    yes    Ke 1993 31.11 24.27 39.87
10    no    Ke 1993 49.09 38.46 62.65
11   yes    Kr 1993 32.67 25.64 41.63
12    no    Kr 1993 51.56 41.68 63.76
13   yes    Ku 1993 31.26 24.47 39.93
14    no    Ku 1993 49.33 39.77 61.19
15   yes    Rd 1993 26.01 20.05 33.74
16    no    Rd 1993 41.04 31.76 53.03
17   yes    Ke 1994 20.80 16.08 26.90
18    no    Ke 1994 32.82 25.42 42.37
19   yes    Kr 1994 21.84 16.52 28.88
20    no    Kr 1994 34.47 26.69 44.52
21   yes    Ku 1994 20.90 15.78 27.69
22    no    Ku 1994 32.98 25.47 42.70
23   yes    Rd 1994 17.39 13.29 22.76
24    no    Rd 1994 27.44 21.00 35.84
25   yes    Ke 1995 27.17 21.05 35.07
26    no    Ke 1995 42.87 33.35 55.11
27   yes    Kr 1995 28.54 22.24 36.62
28    no    Kr 1995 45.03 36.11 56.15
29   yes    Ku 1995 27.30 21.22 35.13
30    no    Ku 1995 43.09 34.46 53.88
31   yes    Rd 1995 22.72 17.39 29.67
32    no    Rd 1995 35.84 27.55 46.63
```

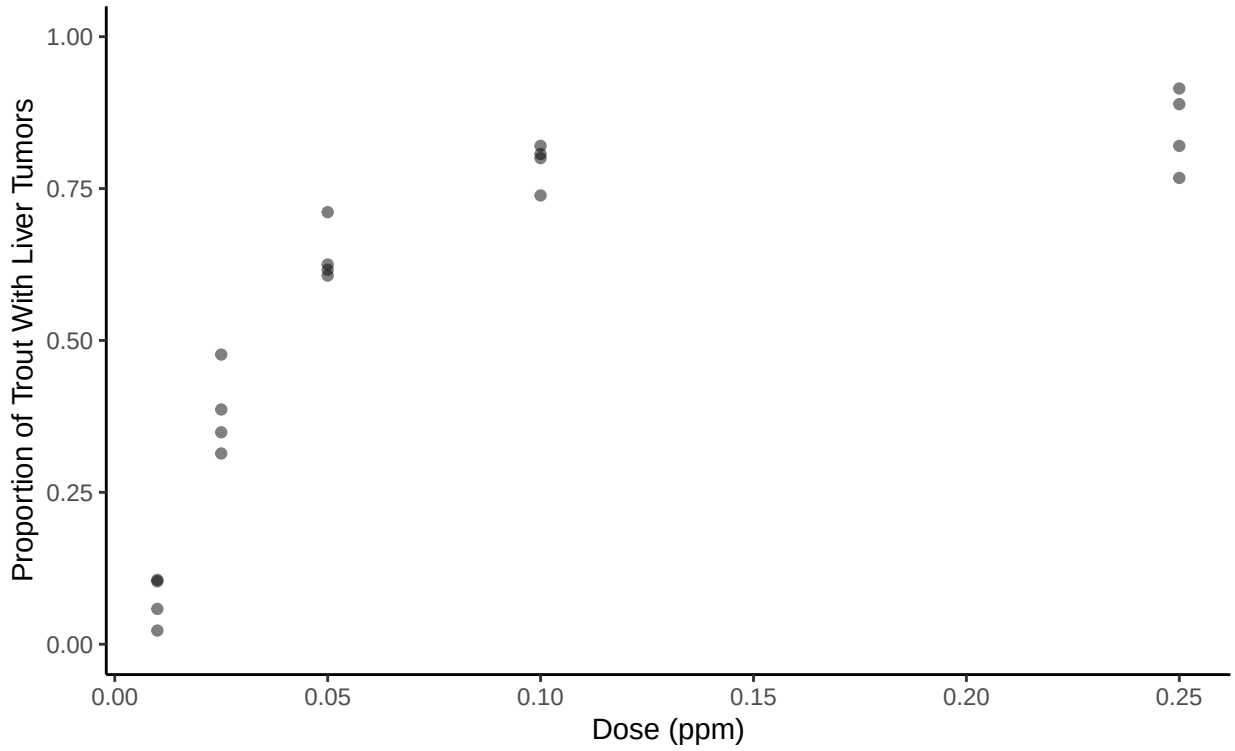
```
d <- cbind(d, glmint(m, newdata = d))
p <- p + geom_pointrange(aes(y = fit, ymin = low, ymax = upp),
  shape = 21, fill = "white", data = d) + geom_point()
plot(p)
```



Aflatoxicol and Liver Tumors in Trout

The data in the data frame `ex2116` in the **Sleuth3** package are from an experiment that investigated the relationship between aflatoxicol and liver tumors in trout. The figure below shows the proportion of trout in each tank that developed liver tumors as well as the dose of aflatoxicol to which the trout were exposed. Aflatoxicol is a metabolite of Aflatoxin B1, a toxic by-product produced by a mold that infects some nuts and grains. Twenty tanks of rainbow trout embryos were exposed to one of five doses of aflatoxicol for one hour. The number of fish in each tank that developed liver tumors one year later was then observed. The plot below shows the data.

```
library(Sleuth3)
library(ggplot2)
p <- ggplot(ex2116, aes(x = Dose, y = Tumor/Total)) +
   geom_point(alpha = 0.5) + theme_classic() + ylim(0, 1) +
   labs(x = "Dose (ppm)", y = "Proportion of Trout With Liver Tumors")
plot(p)
```



The goal here is to estimate the effect of aflatoxicol on the risk of liver tumors in trout. Here we will consider three different logistic regression models.

1. Consider the logistic regression model

$$\log\left[\frac{E(Y_i)}{1-E(Y_i)}\right] = \beta_0 + \beta_1 d_i,$$

where Y_i is the i-th observation of the proportion of trout from a tank that developed liver tumors and d_i is the corresponding dose of aflatoxicol to which those trout were exposed. This model can also be written as

$$E(Y_i) = \frac{e^{\eta_i}}{1+e^{\eta_i}},$$

where $\eta_i = \beta_0 + \beta_1 d_i$. Note that by definition $E(Y_i)$ is also the *probability* that a trout from a given tank will develop liver tumors, and $E(Y_i)/[1-E(Y_i)]$ is the *odds* that a trout from a given tank will develop liver tumors. Estimate this model using `glm`. You should be able to replicate the following results.

```
cbind(summary(m)$coefficients, confint(m))
```

```
            Estimate Std. Error z value  Pr(>|z|)  2.5 %  97.5 %
(Intercept)   -0.867    0.07673   -11.3 1.321e-29 -1.019 -0.7179
Dose          14.334    0.93695    15.3 7.838e-53 12.558 16.2346
```

Next estimate the odds ratio for the effect of increasing dose by 0.05 ppm using the `contrast` function.[3] How is this odds ratio interpreted?

Solution: We can estimate the model as follows.

[3]Here e^{β_1} would be the odds ratio for the effect of increasing dose by 1 ppm. However that is probably not a realistic effect as it would be a relatively large increase in dose. The study only considered up to 0.25 ppm. Using `contrast` is convenient here to estimate the odds ratio for the effect of an arbitrary change in dose.

```
m <- glm(cbind(Tumor, Total - Tumor) ~ Dose, family = binomial, data = ex2116)
summary(m)$coefficients
```

```
            Estimate Std. Error z value  Pr(>|z|)
(Intercept)   -0.867    0.07673   -11.3 1.321e-29
Dose          14.334    0.93695    15.3 7.838e-53
```

The odds ratio can be estimated as follows.

```
trtools::contrast(m,
  a = list(Dose = 0.1),
  b = list(Dose = 0.05), tf = exp)
```

```
 estimate lower upper
    2.048 1.868 2.245
```

```
pairs(emmeans(m, ~Dose, at = list(Dose = c(0.1, 0.05)), type = "response"), infer = TRUE)
```

```
 contrast           odds.ratio     SE  df asymp.LCL asymp.UCL null z.ratio p.value
 Dose0.1 / Dose0.05       2.05 0.0959 Inf      1.87      2.24    1  15.298  <.0001

Confidence level used: 0.95
Intervals are back-transformed from the log odds ratio scale
Tests are performed on the log odds ratio scale
```

2. Now consider a model where we use the base-2 logarithm of dose as the explanatory variable so that

$$\eta_i = \beta_0 + \beta_1 \log_2(d_i).$$

Recall that the function $\log_2$ is known to R as `log2`. Estimate this model using `glm`. You should be able to replicate the following results.

```
cbind(summary(m)$coefficients, confint(m))
```

```
            Estimate Std. Error z value  Pr(>|z|)  2.5 % 97.5 %
(Intercept)   4.1634     0.2085   19.97 9.564e-89 3.7631  4.581
log2(Dose)    0.8997     0.0446   20.17 1.628e-90 0.8141  0.989
```

Here increasing the base-2 logarithm of dose by one unit is the same thing as *doubling* dose, and so the effect on the odds ratio of doubling dose will be the same regardless of what you double (e.g., 0.05 to 1 ppm, 0.1 to 0.2 ppm, etc.).[4] How is this odds ratio interpreted?

Solution: We can estimate the model as follows.

```
m <- glm(cbind(Tumor, Total-Tumor) ~ log2(Dose), family = binomial, data = ex2116)
cbind(summary(m)$coefficients, confint(m))
```

```
            Estimate Std. Error z value  Pr(>|z|)  2.5 % 97.5 %
(Intercept)   4.1634     0.2085   19.97 9.564e-89 3.7631  4.581
log2(Dose)    0.8997     0.0446   20.17 1.628e-90 0.8141  0.989
```

Here is how to estimate the odds ratio for the effect of doubling the dose.

[4] We do not have to use the odds ratio for the effect of doubling dose just because we are using the base-2 logarithm of dose as our explanatory variable. We could also estimate the odds ratio for the effect of increasing dose from, say, 0.05 ppm to 0.1 ppm. But we would need to remember that because we are using the base-2 logarithm of dose as an explanatory variable that this would *not* be the same odds ratio as increasing dose the same amount from, say, 0.1 ppm to 0.15 ppm. Similarly for the previous model where we did not use the base-2 logarithm of dose, we could still estimate the odds ratio for the effect of doubling dose. But here we would need to remember that the odds ratio of doubling from, say, 0.05 ppm to 0.1 ppm would *not* be the same as the odds ratio for doubling from 0.1 ppm to 0.2 ppm.

```
trtools::contrast(m,
  a = list(Dose = 0.2),
  b = list(Dose = 0.1), tf = exp)
```

```
 estimate lower upper
    2.459 2.253 2.684
```

```
pairs(emmeans(m, ~Dose, at = list(Dose = c(0.2, 0.1)), type = "response"), infer = TRUE)
```

```
 contrast          odds.ratio   SE  df asymp.LCL asymp.UCL null z.ratio p.value
 Dose0.2 / Dose0.1       2.46 0.11 Inf      2.25      2.68    1  20.175  <.0001

Confidence level used: 0.95
Intervals are back-transformed from the log odds ratio scale
Tests are performed on the log odds ratio scale
```

3. Rather than trying to decide between using dose or some transformation of dose in the model, we can instead define dose as a 5-level factor. There are two ways we could specify dose as a factor. One would be to create a new variable.

```
ex2116$Dosef <- factor(ex2116$Dose)
```

The levels of `Dosef` will be the original values of `Dose` but converted to strings, which we can see if we use the `levels` function.

```
levels(ex2116$Dosef)
```

```
[1] "0.01"  "0.025" "0.05"  "0.1"   "0.25"
```

Another approach is to replace `Dose` in the model formula with `factor(Dose)`. Use the `contrast` function to estimate the odds ratio for the odds of tumor development at 0.025 ppm versus 0.01 ppm, 0.05 ppm versus 0.01 ppm, 0.1 ppm versus 0.01 ppm, and 0.25 ppm versus 0.01 ppm.[5] How are these odds ratios interpreted?

Solution: Here is how to estimate this model.

```
m <- glm(cbind(Tumor, Total-Tumor) ~ factor(Dose), family = binomial, data = ex2116)
cbind(summary(m)$coefficients, confint(m))
```

```
                  Estimate Std. Error z value  Pr(>|z|)  2.5 % 97.5 %
(Intercept)         -2.556     0.2076 -12.310 8.049e-35 -2.988 -2.171
factor(Dose)0.025    2.073     0.2353   8.809 1.264e-18  1.628  2.553
factor(Dose)0.05     3.132     0.2354  13.306 2.130e-40  2.688  3.614
factor(Dose)0.1      3.890     0.2453  15.857 1.252e-56  3.427  4.391
factor(Dose)0.25     4.260     0.2566  16.605 6.436e-62  3.775  4.784
```

The odds ratios can be estimated as follows.

```
trtools::contrast(m, tf = exp,
  a = list(Dose = c(0.025,0.05,0.1,0.25)),
  b = list(Dose = 0.01))
```

```
 estimate lower  upper
    7.945  5.01  12.60
   22.920 14.45  36.36
   48.909 30.24  79.10
   70.840 42.84 117.13
```

[5] Note that how you specify the levels of dose will depend on whether you created a new variable like `Dosef` or converted it to a factor within the model formula with `factor(Dose)`. For the latter you will need to specify dose as a *number* but if you created it to a new variable you will need to specify it as a *string* by enclosing it in quotes.

```
contrast(emmeans(m, ~Dose, type = "response"), method = "trt.vs.ctrl",
  ref = 1, adjust = "none", infer = TRUE)
```

```
 contrast             odds.ratio    SE  df asymp.LCL asymp.UCL null z.ratio p.value
 Dose0.025 / Dose0.01       7.94  1.87 Inf      5.01      12.6    1   8.809  <.0001
 Dose0.05 / Dose0.01       22.92  5.39 Inf     14.45      36.4    1  13.306  <.0001
 Dose0.1 / Dose0.01        48.91 12.00 Inf     30.24      79.1    1  15.857  <.0001
 Dose0.25 / Dose0.01       70.84 18.18 Inf     42.84     117.1    1  16.605  <.0001

Confidence level used: 0.95
Intervals are back-transformed from the log odds ratio scale
Tests are performed on the log odds ratio scale
```

4. Estimate the odds and probability of tumor development at each value of dose used in the study for any of the three models.

   Solution: For the odds we need to use `contrast` from **trtools**. I am going to use the model from the previous problem.

```
trtools::contrast(m, a = list(Dose = c(0.01,0.025,0.05,0.1,0.25)),
  cnames = c(0.01,0.025,0.05,0.1,0.25), tf = exp)
```

```
      estimate   lower  upper
0.01   0.07764 0.05168 0.1166
0.025  0.61682 0.49654 0.7662
0.05   1.77953 1.43188 2.2116
0.1    3.79730 2.93938 4.9056
0.25   5.50000 4.09298 7.3907
```

   There are several ways to estimate the probabilities.

```
trtools::contrast(m, a = list(Dose = c(0.01,0.025,0.05,0.1,0.25)),
  cnames = c(0.01,0.025,0.05,0.1,0.25), tf = plogis)
```

```
      estimate   lower  upper
0.01   0.07205 0.04914 0.1044
0.025  0.38150 0.33179 0.4338
0.05   0.64023 0.58880 0.6886
0.1    0.79155 0.74615 0.8307
0.25   0.84615 0.80365 0.8808
```

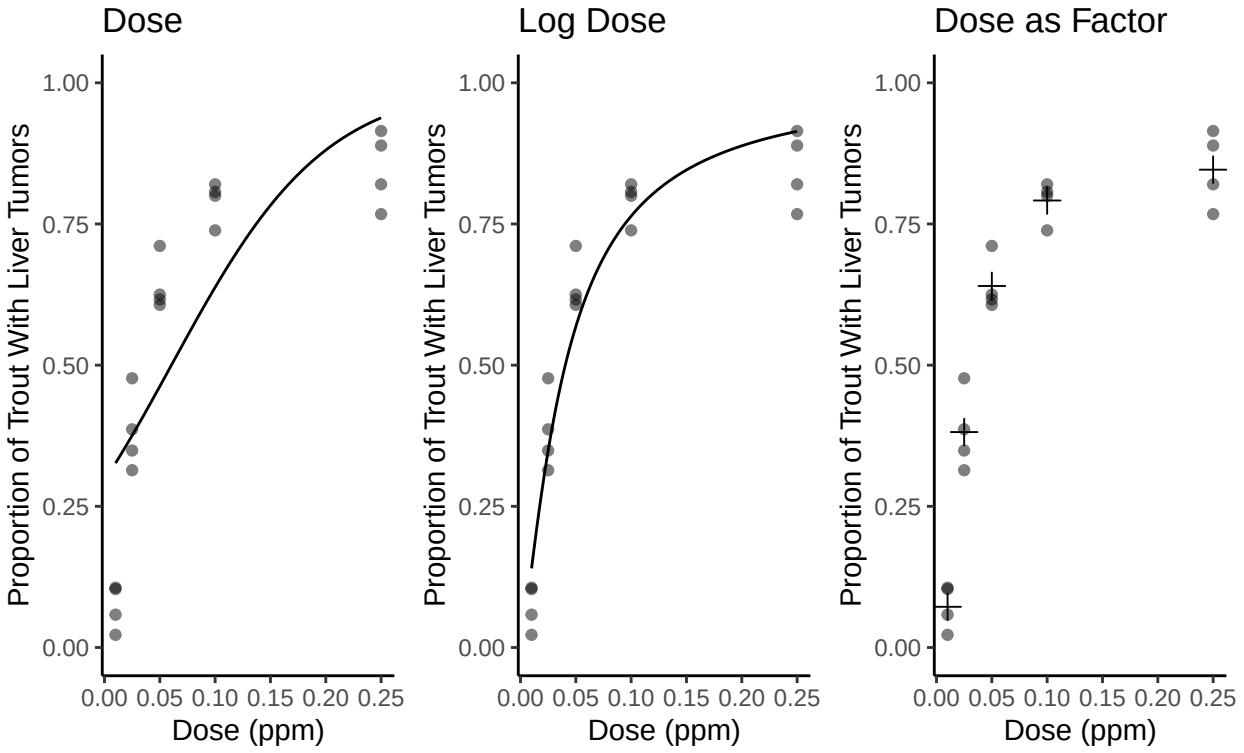
```
emmeans(m, ~Dose, type = "response")
```

```
  Dose  prob     SE  df asymp.LCL asymp.UCL
 0.010 0.072 0.0139 Inf    0.0491     0.104
 0.025 0.382 0.0261 Inf    0.3318     0.434
 0.050 0.640 0.0255 Inf    0.5888     0.689
 0.100 0.791 0.0216 Inf    0.7462     0.831
 0.250 0.846 0.0196 Inf    0.8037     0.881

Confidence level used: 0.95
Intervals are back-transformed from the logit scale
```

Here are plots of the three models we considered for the aflatoxicol data.

```
p <- ggplot(ex2116, aes(x = Dose, y = Tumor/Total)) +
   geom_point(alpha = 0.5) + theme_classic() + ylim(0, 1) +
   labs(x = "Dose (ppm)", y = "Proportion of Trout With Liver Tumors")
```

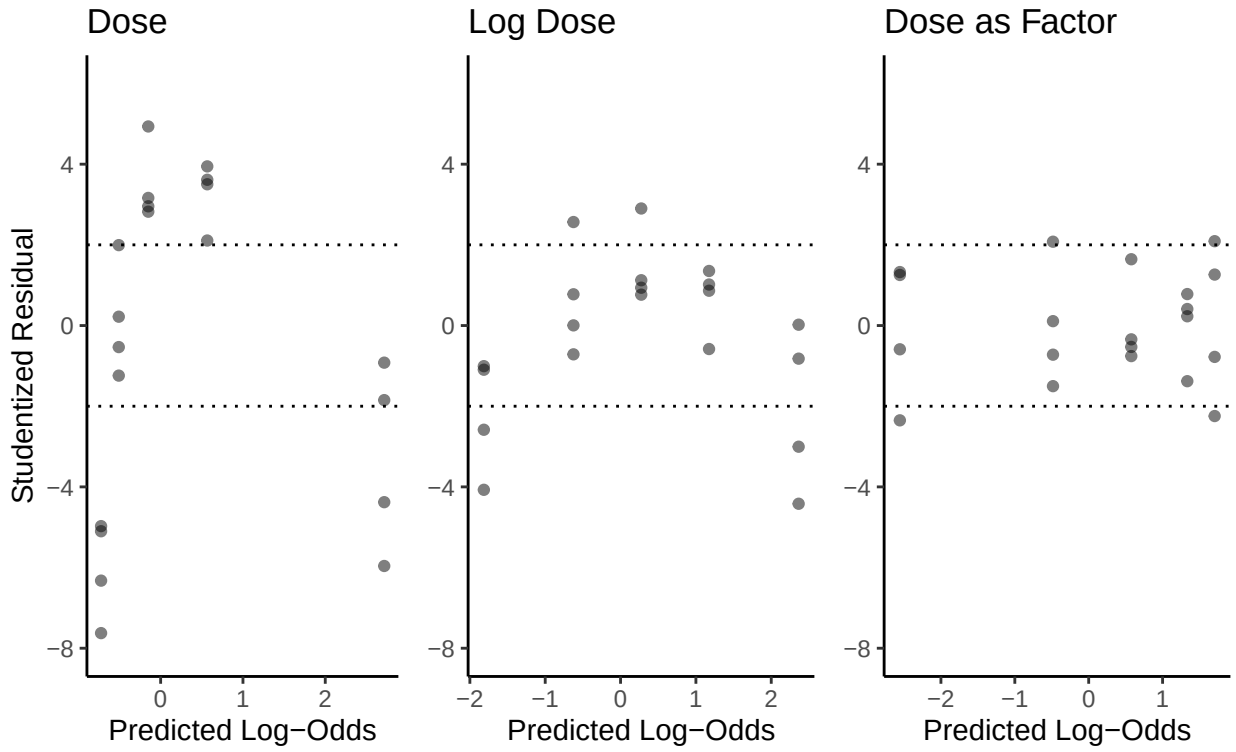
```
m <- glm(cbind(Tumor, Total-Tumor) ~ Dose, family = binomial, data = ex2116)
d <- data.frame(Dose = seq(0.01, 0.25, length = 100))
d$yhat <- predict(m, newdata = d, type = "response")
p1 <- p + geom_line(aes(y = yhat), data = d) + ggtitle("Dose")

m <- glm(cbind(Tumor, Total-Tumor) ~ log2(Dose), family = binomial, data = ex2116)
d <- data.frame(Dose = seq(0.01, 0.25, length = 100))
d$yhat <- predict(m, newdata = d, type = "response")
p2 <- p + geom_line(aes(y = yhat), data = d) + ggtitle("Log Dose")

m <- glm(cbind(Tumor, Total-Tumor) ~ factor(Dose), family = binomial, data = ex2116)
d <- data.frame(Dose = unique(ex2116$Dose))
d$yhat <- predict(m, newdata = d, type = "response")
p3 <- p + geom_point(aes(y = yhat), data = d, pch = 3, size = 3) + ggtitle("Dose as Factor")

cowplot::plot_grid(p1, p2, p3, nrow = 1)
```



Note that the three models do not appear to fit the data equally well. Using the logarithm of dose as an explanatory variable appears to be a better fit than using dose, but both models appear to systematically over-estimate or under-estimate the probability of tumor development. Treating dose as a factor may be a better model here. This is even more clear when looking at residual plots.

```
m1 <- glm(cbind(Tumor, Total-Tumor) ~ Dose, family = binomial, data = ex2116)
m2 <- glm(cbind(Tumor, Total-Tumor) ~ log2(Dose), family = binomial, data = ex2116)
m3 <- glm(cbind(Tumor, Total-Tumor) ~ factor(Dose), family = binomial, data = ex2116)

d1 <- ex2116
d1$yhat <- predict(m1)
d1$residual <- rstudent(m1)
```

```
d2 <- ex2116
d2$yhat <- predict(m2)
d2$residual <- rstudent(m2)

d3 <- ex2116
d3$yhat <- predict(m3)
d3$residual <- rstudent(m3)

p <- ggplot(d1, aes(x = yhat, y = residual)) + theme_classic() +
  geom_point(alpha = 0.5) + ylim(-8,6) +
  geom_hline(yintercept = c(-2,2), linetype = 3) +
  labs(x = "Predicted Log-Odds", y = "Studentized Residual")
p1 <- p + ggtitle("Dose")

p <- ggplot(d2, aes(x = yhat, y = residual)) + theme_classic() +
  geom_point(alpha = 0.5) + ylim(-8,6) +
  geom_hline(yintercept = c(-2,2), linetype = 3) +
  labs(x = "Predicted Log-Odds", y = NULL)
p2 <- p + ggtitle("Log Dose")

p <- ggplot(d3, aes(x = yhat, y = residual)) + theme_classic() +
  geom_point(alpha = 0.5) + ylim(-8,6) +
  geom_hline(yintercept = c(-2,2), linetype = 3) +
  labs(x = "Predicted Log-Odds", y = NULL)
p3 <- p + ggtitle("Dose as Factor")

cowplot::plot_grid(p1, p2, p3, nrow = 1)
```



Based on the residuals, the model with dose as a factor appears to provide the best fit to the data. But there may be another model that uses dose as a quantitative explanatory variable (i.e., not a factor) that would be

a good fit to these data.