# Examples Volume 1 

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## References:

Sorry - an on-line version of the references is currently unavailable.

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Please refer to the existing Examples documentation available from http://www.mrc-bsu.cam.ac.uk/bugs.

## Rats: a normal hierarchical model

This example is taken from section 6 of Gelfand et al (1990), and concerns 30 young rats whose weights were measured weekly for five weeks. Part of the data is shown below, where $\mathrm{Y}_{\mathrm{ij}}$ is the weight of the ith rat measured at age $x_{j}$.

|  | Weights $Y_{i j}$ of rat $i$ on day $x_{j}$ |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
|  | $x_{\mathrm{j}}=8$ | 15 | 22 | 29 | 36 |
| Rat 1 | 151 | 199 | 246 | 283 | 320 |
| Rat 2 | 145 | 199 | 249 | 293 | 354 |
| स.... |  |  |  |  |  |
| Rat 30 | 153 | 200 | 244 | 286 | 324 |

A plot of the 30 growth curves suggests some evidence of downward curvature.
The model is essentially a random effects linear growth curve

$$
\begin{aligned}
& \mathrm{Y}_{\mathrm{ij}} \sim \operatorname{Normal}\left(\alpha_{\mathrm{i}}+\beta_{\mathrm{i}}\left(\mathrm{x}_{\mathrm{j}}-\mathrm{x}_{\mathrm{bar}}\right), \tau_{\mathrm{c}}\right) \\
& \alpha_{\mathrm{i}} \sim \operatorname{Normal}\left(\alpha_{\mathrm{c}}, \tau_{\alpha}\right) \\
& \beta_{\mathrm{i}} \sim \operatorname{Normal}\left(\beta_{\mathrm{c}}, \tau_{\beta}\right)
\end{aligned}
$$

where $\mathrm{x}_{\mathrm{bar}}=22$, and $\tau$ represents the precision ( $1 /$ variance) of a normal distribution. We note the absence of a parameter representing correlation between $\alpha_{i}$ and $\beta_{i}$ unlike in Gelfand et al 1990. However, see the Birats example in Volume 2 which does explicitly model the covariance between $\alpha_{i}$ and $\beta_{i}$. For now, we standardise the $x_{j}$ 's around their mean to reduce dependence between $\alpha_{i}$ and $\beta_{i}$ in their likelihood: in fact for the full balanced data, complete independence is achieved. (Note that, in general, prior independence does not force the posterior distributions to be independent).
$\alpha_{\mathrm{c}}, \tau_{\alpha}, \beta_{\mathrm{c}}, \tau_{\beta}, \tau_{\mathrm{c}}$ are given independent "noninformative" priors. Interest particularly focuses on the intercept at zero time (birth), denoted $\alpha_{0}=\alpha_{c}-\beta_{c} x_{b a r}$.

## Graphical model for rats example:



BUGS language for rats example:

```
model
{
    for(i in 1:N ) {
        for(j in 1:T){
            Y[i , j] ~ dnorm(mu[i , j],tau.c)
            mu[i, j] <- alpha[i] + beta[i] * (x[j] - xbar)
        }
        alpha[i] ~ dnorm(alpha.c,alpha.tau)
        beta[i] ~ dnorm(beta.c,beta.tau)
    }
    tau.c ~ dgamma(0.001,0.001)
    sigma <- 1 / sqrt(tau.c)
    alpha.c ~ dnorm(0.0,1.0E-6)
    alpha.tau ~ dgamma(0.001,0.001)
    beta.c ~ dnorm(0.0,1.0E-6)
    beta.tau ~ dgamma(0.001,0.001)
    alpha0 <- alpha.c - xbar * beta.c
}
```

Note the use of a very flat but conjugate prior for the population effects: a locally uniform prior
could also have been used.

## Data ( click to open )

Inits ( click to open )
(Note: the response data ( Y ) for the rats example can also be found in the file ratsy.odc in rectangular format. The covariate data ( X ) can be found in S-Plus format in file ratsx.odc. To load data from each of these files, focus the window containing the open data file before clicking on "load data" from the "Specification" dialog.)

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates:

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| alpha0 | 106.6 | 3.655 | 0.04079 | 99.44 | 106.5 | 113.8 | 1001 |
| beta.c | 6.185 | 0.1061 | 0.00132 | 5.975 | 6.185 | 6.394 | 1001 |
| sigma | 6.086 | 0.4606 | 0.007398 | 5.255 | 6.061 | 7.049 | 1001 |

These results may be compared with Figure 5 of Gelfand et al 1990 --- we note that the mean gradient of independent fitted straight lines is 6.19.

Gelfand et al 1990 also consider the problem of missing data, and delete the last observation of cases $6-10$, the last two from 11-20, the last 3 from 21-25 and the last 4 from 26-30. The appropriate data file is obtained by simply replacing data values by NA (see below). The model specification is unchanged, since the distinction between observed and unobserved quantities is made in the data file and not the model specification.

## Data ( click to open )

Gelfand et al 1990 focus on the parameter estimates and the predictions for the final 4 observations on rat 26 . These predictions are obtained automatically in BUGS by monitoring the relevant $Y \square$ nodes. The following estimates were obtained:

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| $\mathrm{Y}[26,2]$ | 204.6 | 8.689 | 0.1145 | 187.6 | 204.7 | 221.4 | 1001 | 10000 |
| $\mathrm{Y}[26,3]$ | 250.2 | 10.21 | 0.1732 | 230.1 | 250.2 | 270.5 | 1001 | 10000 |
| $\mathrm{Y}[26,4]$ | 295.6 | 12.5 | 0.228 | 270.6 | 295.5 | 319.7 | 1001 | 10000 |
| $\mathrm{Y}[26,5]$ | 341.2 | 15.29 | 0.2936 | 310.7 | 341.3 | 370.9 | 1001 | 10000 |
| beta.c | 6.578 | 0.1497 | 0.003415 | 6.284 | 6.578 | 6.87 | 1001 | 10000 |

We note that our estimate 6.58 of $\beta_{c}$ is substantially greater than that shown in Figure 6 of Gelfand et al 1990. However, plotting the growth curves indicates some curvature with steeper gradients at the beginning: the mean of the estimated gradients of the reduced data is 6.66 , compared to 6.19 for the full data. Hence we are inclined to believe our analysis. The observed
weights for rat 26 were 207, 257, 303 and 345 , compared to our predictions of 204, 250, 295 and 341.

## Dogs: loglinear model for binary data

Lindley (19??) analyses data from Kalbfleisch (1985) on the Solomon-Wynne experiment on dogs, whereby they learn to avoid an electric shock. A dog is put in a compartment, the lights are turned out and a barrier is raised, and 10 seconds later an electric shock is applied. The results are recorded as success $(Y=1)$ if the dog jumps the barrier before the shock occurs, or failure ( $\mathrm{Y}=0$ ) otherwise.

Thirty dogs were each subjected to 25 such trials. A plausible model is to suppose that a dog learns from previous trials, with the probability of success depending on the number of previous shocks and the number of previous avoidances. Lindley thus uses the following model

$$
\pi_{j}=A^{x_{j}} B^{j-x_{j}}
$$

for the probability of a shock (failure) at trial $j$, where $x_{j}=$ number of success (avoidances) before trial j and $\mathrm{j}-\mathrm{x}_{\mathrm{j}}=$ number of previous failures (shocks). This is equivalent to the following log linear model

$$
\log \pi_{j}=\alpha x_{j}+\beta\left(j-x_{j}\right)
$$

Hence we have a generalised linear model for binary data, but with a log-link function rather than the canonical logit link. This is trivial to implement in BUGS:

```
model
{
    for (i in 1 : Dogs) {
        xa[i, 1] <- 0; xs[i, 1] <- 0 p[i, 1] <- 0
        for (j in 2:Trials) {
            xa[i, j] <- sum(Y[i, 1 : j - 1])
            xs[i, j] <- j - 1 - xa[i, j]
            log(p[i, j]) <- alpha * xa[i, j] + beta * xs[i, j]
            y[i, j] <- 1 - Y[i, j]
            y[i, j] ~ dbern(p[i, j])
        }
    }
    alpha ~ dnorm(0, 0.00001)I(, -0.00001)
    beta ~ dnorm(0, 0.00001)l(, -0.00001)
    A <- exp(alpha)
    B<- exp(beta)
}
```


## Data (click to open)

## Inits( click to open )

## Results

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| A | 0.7833 | 0.01917 | $2.665 \mathrm{E}-4$ | 0.746 | 0.7833 | 0.8207 | 1001 | 10000 |
| B | 0.9242 | 0.01089 | $1.573 \mathrm{E}-4$ | 0.9018 | 0.9247 | 0.9445 | 1001 | 10000 |
| alpha | -0.2446 | 0.02451 | $3.4 \mathrm{E}-4$ | -0.293 | -0.2442 | -0.1976 | 1001 | 10000 |
| beta | -0.07886 | 0.0118 | $1.705 \mathrm{E}-4$ | -0.1033 | -0.07825 | -0.05711 | 1001 | 10000 |

## Seeds: Random effect logistic regression

This example is taken from Table 3 of Crowder (1978), and concerns the proportion of seeds that germinated on each of 21 plates arranged according to a 2 by 2 factorial layout by seed and type of root extract. The data are shown below, where $r_{i}$ and $n_{i}$ are the number of germinated and the total number of seeds on the $i$ th plate, $i=1, \ldots, \mathrm{~N}$. These data are also analysed by, for example, Breslow: and Clayton (1993).

| r | seed O. aegyptiaco 75 |  |  |  |  | seed O. aegyptiaco 73 |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Bean |  |  | Cucumber |  | r | Bean |  | r | Cucumber |  |
|  | n | r/n | $r$ | n | r/n |  | n | r/n |  | n | r/n |
| 10 | 39 | 0.26 | 5 | 6 | 0.83 | 8 | 16 | 0.50 | 3 | 12 | 0.25 |
| 23 | 62 | 0.37 | 53 | 74 | 0.72 | 10 | 30 | 0.33 | 22 | 41 | 0.54 |
| 23 | 81 | 0.28 | 55 | 72 | 0.76 | 8 | 28 | 0.29 | 15 | 30 | 0.50 |
| 26 | 51 | 0.51 | 32 | 51 | 0.63 | 23 | 45 | 0.51 | 32 | 51 | 0.63 |
| 17 | 39 | 0.44 | 46 | 79 | 0.58 | 0 | 4 | 0.00 | 3 | 7 | 0.43 |
|  |  |  | 10 | 13 | 0.77 |  |  |  |  |  |  |

The model is essentially a random effects logistic, allowing for over-dispersion. If $p_{i}$ is the probability of germination on the $i$ th plate, we assume

$$
\begin{aligned}
& r_{i} \sim \operatorname{Binomial}\left(p_{i}, n_{i}\right) \\
& \operatorname{logit}\left(p_{i}\right)=\alpha_{0}+\alpha_{1} x_{1 i}+\alpha_{2} x_{2 i}+\alpha_{12} x_{1 i} x_{2 i}+b_{i} \\
& b_{i} \sim \operatorname{Normal}(0, \tau)
\end{aligned}
$$

where $\mathrm{x}_{1 \mathrm{i}}, \mathrm{x}_{2 \mathrm{i}}$ are the seed type and root extract of the $i$ th plate, and an interaction term $\alpha_{12} x_{1 i} x_{2 i}$ is included. $\alpha_{0}, \alpha_{1}, \alpha_{2}, \alpha_{12}, \tau$ are given independent "noninformative" priors.


## BUGS language for seeds example

```
model
{
    for(i in 1:N ) {
        r[i] ~ dbin(p[i],n[i])
        b[i] ~ dnorm(0.0,tau)
        logit(p[i]) <- alpha0 + alpha1 * x1[i] + alpha2 * x2[i] +
            alpha12 * x1[i] * x2[i] + b[i]
    }
    alpha0 ~ dnorm(0.0,1.0E-6)
    alpha1 ~ dnorm(0.0,1.0E-6)
    alpha2 ~ dnorm(0.0,1.0E-6)
    alpha12 ~ dnorm(0.0,1.0E-6)
    tau ~ dgamma(0.001,0.001)
    sigma <- 1 / sqrt(tau)
}
```


## Data ( click to open )

Inits ( click to open )

## Results

A burn in of 1000 updates followed by a further 10000 updates gave the following parameter estimates:

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc start | sample |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| alpha0 | -0.5525 | 0.1852 | 0.00402 | -0.9312 | -0.5505 | -0.1879 | 1001 | 10000 |
| alpha1 | 0.08382 | 0.3031 | 0.005803 | -0.5238 | 0.09076 | 0.6794 | 1001 | 10000 |
| alpha12 | -0.8165 | 0.4109 | 0.008128 | -1.671 | -0.8073 | -0.0287 | 1001 | 10000 |
| alpha2 | 1.346 | 0.2564 | 0.00553 | 0.8501 | 1.34 | 1.881 | 1001 | 10000 |
| sigma | 0.267 | 0.1471 | 0.007996 | 0.03842 | 0.2552 | 0.5929 | 1001 | 10000 |

We may compare simple logistic, maximum likelihood (from EGRET), penalized quasi-likelihood (PQL) Breslow and Clayton (1993) with the BUGS results

| variable | Logistic regression $\beta$ SE | maximum <br> likelihood <br> $\beta$ SE | $\begin{aligned} & \text { PQL } \\ & \beta \quad \mathrm{SE} \end{aligned}$ |
| :---: | :---: | :---: | :---: |
| $\alpha_{0}$ | -0.558 0.126 | -0.546 0.167 | -0.542 0.190 |
| $\alpha_{1}$ | 0.146 | 0.0970 .278 | 0.77 |
| $\alpha_{2}$ | 1.3180 .177 | 1.3370 .237 | 1.3390 .270 |
| $\alpha_{12}$ | -0.778 0.306 | -0.811 0.385 | -0.825 0.430 |
| ${ }_{\sigma}$ | --- --- | 0.2360 .110 | 0.3130 .121 |

Heirarchical centering is an interesting reformulation of random effects models. Introduce the variables

$$
\begin{aligned}
& \mu_{i}=\alpha_{0}+\alpha_{1} x_{1 i}+\alpha_{2} x_{2 i}+\alpha_{12} x_{1 i} x_{2 i} \\
& \beta_{i}=\mu_{i}+b_{i}
\end{aligned}
$$

the model then becomes

$$
\begin{aligned}
& r_{i} \sim \operatorname{Binomial}\left(p_{i}, n_{i}\right) \\
& \operatorname{logit}\left(p_{i}\right)=\beta_{i}
\end{aligned}
$$

$$
\beta_{\mathrm{i}} \sim \operatorname{Normal}\left(\mu_{\mathrm{i}}, \tau\right)
$$

The graphical model is shown below


This formulation of the model has two advantages: the squence of random numbers generated by the Gibbs sampler has better correlation properties and the time per update is reduced because the updating for the $\alpha$ parameters is now conjugate.

## Surgical: Institutional ranking

This example considers mortality rates in 12 hospitals performing cardiac surgery in babies. The data are shown below.

| Hospital | No of ops | No of deaths |
| :--- | :--- | :--- |
| A | 47 | 0 |
| B | 148 | 18 |
| C | 119 | 8 |
| D | 810 | 46 |
| E | 211 | 8 |
| F | 196 | 13 |
| G | 148 | 9 |
| H | 215 | 31 |
| l | 207 | 14 |
| J | 97 | 8 |
| K | 256 | 29 |
| L | 360 | 24 |

The number of deaths $r_{i}$ for hospital $i$ are modelled as a binary response variable with 'true' failure probability $\mathrm{p}_{\mathrm{i}}$ :

$$
\mathrm{r}_{\mathrm{i}} \sim \operatorname{Binomial}\left(\mathrm{p}_{\mathrm{i}}, \mathrm{n}_{\mathrm{i}}\right)
$$

We first assume that the true failure probabilities are independent (i.e.fixed effects) for each hospital. This is equivalent to assuming a standard non-informative prior distribution for the $\mathrm{p}_{\mathrm{i}} \mathrm{s}$, namely:

$$
\mathrm{p}_{\mathrm{i}} \sim \operatorname{Beta}(1.0,1.0)
$$

Graphical model for fixed effects surgical example:


BUGS language for fixed effects surgical model:

```
model
{
    for(i in 1:N ) {
        p[i] ~ dbeta(1.0, 1.0)
        r[i] ~ dbin(p[i], n[i])
    }
}
```


## Data ( click to open )

## Inits ( click to open )

A more realistic model for the surgical data is to assume that the failure rates across hospitals are similar in some way. This is equivalent to specifying a random effects model for the true failure probabilities $\mathrm{p}_{\mathrm{i}}$ as follows:

$$
\begin{aligned}
& \operatorname{logit}\left(p_{i}\right)=b_{i} \\
& \mathrm{~b}_{\mathrm{i}} \sim \operatorname{Normal}(\mu, \tau)
\end{aligned}
$$

Standard non-informative priors are then specified for the population mean (logit) probability of failure, $\mu$, and precision, $\tau$.


BUGS language for random effects surgical model:

```
model
{
    for(i in 1:N ) {
        b[i] ~ dnorm(mu,tau)
        r[i] ~ dbin(p[i],n[i])
        logit(p[i]) <- b[i]
        }
    pop.mean <- exp(mu)/ (1 + exp(mu))
    mu ~ dnorm(0.0,1.0E-6)
    sigma <- 1 / sqrt(tau)
    tau ~ dgamma(0.001,0.001)
}
```

Data (click to open)
Inits ( click to open )

## Results

A burn in of 1000 updates followed by a further 10000 updates gave the following estimates of surgical mortality in each hospital for the fixed effect analysis

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc | start | sample |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| $\mathrm{p}[1]$ | 0.02009 | 0.01946 | $2.085 \mathrm{E}-4$ | $6.091 \mathrm{E}-4$ | 0.01441 | 0.07178 | 1001 | 10000 |
| $\mathrm{p}[2]$ | 0.1266 | 0.0271 | $2.67 \mathrm{E}-4$ | 0.07853 | 0.125 | 0.1845 | 1001 | 10000 |
| $\mathrm{p}[3]$ | 0.07436 | 0.02371 | $2.349 \mathrm{E}-4$ | 0.03492 | 0.07181 | 0.1265 | 1001 | 10000 |
| $\mathrm{p}[4]$ | 0.05789 | 0.00824 | $8.136 \mathrm{E}-5$ | 0.04264 | 0.05762 | 0.07487 | 1001 | 10000 |
| $\mathrm{p}[5]$ | 0.04237 | 0.01388 | $1.096 \mathrm{E}-4$ | 0.01972 | 0.04086 | 0.07362 | 1001 | 10000 |
| $\mathrm{p}[6]$ | 0.07081 | 0.01811 | $1.935 \mathrm{E}-4$ | 0.0397 | 0.06931 | 0.1098 | 1001 | 10000 |
| $\mathrm{p}[7]$ | 0.06686 | 0.02025 | $1.872 \mathrm{E}-4$ | 0.03259 | 0.06493 | 0.111 | 1001 | 10000 |
| $\mathrm{p}[8]$ | 0.1473 | 0.02393 | $2.681 \mathrm{E}-4$ | 0.1039 | 0.146 | 0.1983 | 1001 | 10000 |
| $\mathrm{p}[9]$ | 0.07216 | 0.0179 | $1.59 \mathrm{E}-4$ | 0.04093 | 0.07071 | 0.1104 | 1001 | 10000 |
| $\mathrm{p}[10]$ | 0.09078 | 0.0288 | $3.122 \mathrm{E}-4$ | 0.04274 | 0.08817 | 0.1531 | 1001 | 10000 |
| $\mathrm{p}[11]$ | 0.1165 | 0.02009 | $2.074 \mathrm{E}-4$ | 0.08 | 0.1155 | 0.1589 | 1001 | 10000 |
| $\mathrm{p}[12]$ | 0.06906 | 0.01345 | $1.261 \mathrm{E}-4$ | 0.04518 | 0.06816 | 0.0977 | 1001 | 10000 |

and for the random effects analysis

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc | start | sample |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| mu | -2.558 | 0.1554 | 0.002585 | -2.884 | -2.551 | -2.266 | 1001 | 10000 |
| $\mathrm{p}[1]$ | 0.05302 | 0.01948 | $3.565 \mathrm{E}-4$ | 0.01802 | 0.05221 | 0.09348 | 1001 | 10000 |
| $\mathrm{p}[2]$ | 0.1029 | 0.02196 | $2.976 \mathrm{E}-4$ | 0.06712 | 0.1006 | 0.152 | 1001 | 10000 |
| $\mathrm{p}[3]$ | 0.07044 | 0.01727 | $1.978 \mathrm{E}-4$ | 0.0397 | 0.06916 | 0.1079 | 1001 | 10000 |
| $\mathrm{p}[4]$ | 0.0593 | 0.007985 | $1.212 \mathrm{E}-4$ | 0.04458 | 0.05897 | 0.07591 | 1001 | 10000 |
| $\mathrm{p}[5]$ | 0.05187 | 0.01329 | $2.269 \mathrm{E}-4$ | 0.02791 | 0.05102 | 0.07961 | 1001 | 10000 |
| $\mathrm{p}[6]$ | 0.06903 | 0.01448 | $1.564 \mathrm{E}-4$ | 0.04284 | 0.06854 | 0.1004 | 1001 | 10000 |
| $\mathrm{p}[7]$ | 0.06682 | 0.01602 | $1.773 \mathrm{E}-4$ | 0.03835 | 0.06595 | 0.1009 | 1001 | 10000 |
| $\mathrm{p}[8]$ | 0.1226 | 0.02244 | $4.014 \mathrm{E}-4$ | 0.08196 | 0.1217 | 0.1698 | 1001 | 10000 |
| $\mathrm{p}[9]$ | 0.0698 | 0.01432 | $1.508 \mathrm{E}-4$ | 0.04432 | 0.06901 | 0.1004 | 1001 | 10000 |
| $\mathrm{p}[10]$ | 0.07851 | 0.01955 | $2.03 \mathrm{E}-4$ | 0.04506 | 0.07662 | 0.1217 | 1001 | 10000 |
| $\mathrm{p}[11]$ | 0.1021 | 0.01761 | $2.283 \mathrm{E}-4$ | 0.07158 | 0.1009 | 0.1398 | 1001 | 10000 |
| $\mathrm{p}[12]$ | 0.06858 | 0.01168 | $1.301 \mathrm{E}-4$ | 0.04745 | 0.06805 | 0.09349 | 1001 | 10000 |
| pop. mean | 0.07259 | 0.01028 | $1.696 \mathrm{E}-4$ | 0.05293 | 0.07235 | 0.09401 | 1001 | 10000 |
| sigma | 0.4028 | 0.16 | 0.003672 | 0.1577 | 0.3793 | 0.7872 | 1001 | 10000 |

A particular strength of the Markov chain Monte Carlo (Gibbs sampling) approach implemented in BUGS is the ability to make inferences on arbitrary functions of unknown model parameters. For example, we may compute the rank probabilty of failure for each hospital at each iteration. This yields a sample from the posterior distribution of the ranks.

The figures below show the posterior ranks for the estimated surgical mortality rate in each hospital for the random effect models. These are obtained by setting the rank monitor for variable p (select the "Rank" option from the "Statistics" menu) after the burn-in phase, and then selecting the "histogram" option from this menu after a further 10000 updates. These distributions illustrate the considerable uncertainty associated with 'league tables': there are only 2 hospitals (H and K) whose intervals exclude the median rank and none whose intervals fall completely within the lower or upper quartiles.

Plots of distribution of ranks of true failure probability for random effects model:


## Salm: extra - Poisson variation in dose - response study

Breslow (1984) analyses some mutagenicity assay data (shown below) on salmonella in which three plates have been processed at each dose $i$ of quinoline and the number of revertant colonies of TA98 Salmonella measured. A certain dose-response curve is suggested by theory.

$$
\text { dose of quinoline ( } \mu \mathrm{g} \text { per plate) }
$$

| 0 | 10 | 33 | 100 | 333 | 1000 |
| :--- | :--- | :--- | :--- | :--- | :--- |
| 15 | 16 | 16 | 27 | 33 | 20 |
| 21 | 18 | 26 | 41 | 38 | 27 |
| 29 | 21 | 33 | 69 | 41 | 42 |

This is assumed to be a random effects Poisson model allowing for over-dispersion. Let $x_{i}$ be the dose on the plates $i 1, i 2$ and $i 3$. Then we assume

$$
\begin{aligned}
& y_{\mathrm{ij}} \sim \operatorname{Poisson}\left(\mu_{\mathrm{ij}}\right) \\
& \log \left(\mu_{\mathrm{ij}}\right)=\alpha+\beta \log \left(\mathrm{x}_{\mathrm{i}}+10\right)+\gamma \mathrm{x}_{\mathrm{i}}+\lambda_{\mathrm{ij}} \\
& \lambda_{\mathrm{ij}} \sim \operatorname{Normal}(0, \tau)
\end{aligned}
$$

$\alpha, \beta, \gamma, \tau$ are given independent "noninformative" priors. The appropriate graph is shown


## BUGS language for salm example

```
model
{
    for(i in 1: doses ){
        for( j in 1 : plates ) {
            y[i, j] ~ dpois(mu[i, j])
            log(mu[i, ,j) <- alpha + beta * log(x[i] + 10) +
                gamma * x[i] + lambda[i , j]
            lambda[i , j] ~ dnorm(0.0, tau)
        }
    }
    alpha ~ dnorm(0.0,1.0E-6)
    beta ~ dnorm(0.0,1.0E-6)
    gamma ~ dnorm(0.0,1.0E-6)
    tau ~ dgamma(0.001, 0.001)
    sigma <- 1 / sqrt(tau)
}
```

Data ( click to open)
Inits ( click to open)

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc |  | median | val97.5pc start | sample |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| alpha | 2.193 | 0.3874 | 0.01118 | 1.438 | 2.194 | 2.959 | 1001 | 10000 |
| beta | 0.3059 | 0.1054 | 0.003266 | 0.09692 | 0.3065 | 0.5131 | 1001 | 10000 |
| gamma | $-9.577 \mathrm{E}-4$ | $4.525 \mathrm{E}-4$ | $1.48 \mathrm{E}-5$ | -0.001837 | $-9.622 \mathrm{E}-4$ | $-3.196 \mathrm{E}-5$ | 1001 | 10000 |
| sigma | 0.2608 | 0.08077 | 0.002114 | 0.1305 | 0.2512 | 0.4472 | 1001 | 10000 |

These estimates can be compared with the quasi-likelihood estimates of Breslow (1984) who reported $\alpha=2.203+/-0.363, \beta=0.311+/-0.099, \gamma=-9.74 \mathrm{E}-4+/-4.37 \mathrm{E}-4, \sigma=0.268$

## Equiv: bioequivalence in a cross-over trial

The table below shows some data from a two-treatment, two-period crossover trial to compare 2 tablets A and B, as reported by Gelfand et al (1990).

| Subject $i$ | Sequence | seq | Period 1 | $\mathrm{T}_{\mathrm{i} 1}$ | Period 2 | $\mathrm{T}_{\mathrm{i} 2}$ |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| 1 |  |  |  |  |  |  |
| 2 | AB | 1 | 1.40 | 1 | 1.65 | 2 |
| 3 | AB | 1 | 1.64 | 1 | 1.57 | 2 |
| $\ldots$. | BA | -1 | 1.44 | 2 | 1.58 | 1 |
| 8 | AB |  |  |  |  |  |
| 9 | BA | -1 | 1.25 | 1 | 1.44 | 2 |
| 10 | BA | -1 | 1.25 | 2 | 1.39 | 1 |
|  |  |  |  |  | 2 | 1.52 |

The response $Y_{i k}$ from the $i$ th subject $(i=1, \ldots, 10)$ in the $k$ th period $(k=1,2)$ is assumed to be of the form

$$
\begin{aligned}
& \mathrm{Y}_{\mathrm{ik}} \sim \operatorname{Normal}\left(\mathrm{~m}_{\mathrm{ik}}, \tau_{1}\right) \\
& \mathrm{m}_{\mathrm{ik}}=\mu+(-1)^{\mathrm{T}_{\mathrm{ik}}-1} \phi / 2+(-1)^{\mathrm{k}-1} \pi / 2+\delta_{\mathrm{i}} \\
& \delta_{\mathrm{i}} \sim \operatorname{Normal}\left(0, \tau_{2}\right)
\end{aligned}
$$

where $\mathrm{T}_{\mathrm{ik}}=1,2$ denotes the treatment given to subject $i$ in period $k, \mu, \phi, \pi$ are the overall mean, treatment and period effects respectively, and $\delta_{i}$ represents the random effect for subject $i$. The graph of this model and its BUGS language description are shown below

Graphical model for equiv example


## BUGS language for equiv example

```
model
{
    for(k in 1:P ) {
            for(i in 1:N ) {
            Y[i,k] ~ dnorm(m[i, k], tau1)
            m[i , k] <- mu + sign[T[i , k]] * phi / 2 + sign[k] * pi / 2 + delta[i]
            T[i,k]<- group[i] * (k - 1.5) + 1.5
        }
    }
    for(i in 1:N ) {
        delta[i] ~ dnorm(0.0, tau2)
    }
    tau1 ~ dgamma(0.001, 0.001) sigma1 <- 1 / sqrt(tau1)
    tau2 ~ dgamma(0.001, 0.001) sigma2 <- 1 / sqrt(tau2)
    mu ~ dnorm(0.0, 1.0E-6)
    phi ~ dnorm(0.0, 1.0E-6)
    pi ~ dnorm(0.0, 1.0E-6)
    theta <- exp(phi)
    equiv <- step(theta - 0.8) - step(theta - 1.2)
}
```

Note the use of the step function to indicate whether $\theta=e^{\phi}$ lies between 0.8 and 1.2
which traditionally determines bioequivelence.

## Data ( click to open)

## Inits ( click to open )

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameteres estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| equiv | 0.9976 | 0.04893 | $5.148 \mathrm{E}-4$ | 1.0 | 1.0 | 1.0 | 1001 | 10000 |
| mu | 1.437 | 0.05364 | 0.001822 | 1.329 | 1.437 | 1.542 | 1001 | 10000 |
| phi | -0.008338 | 0.05201 | $5.151 \mathrm{E}-4$ | -0.1127 | -0.008502 | 0.09926 | 1001 | 10000 |
| pi | -0.1802 | 0.05189 | $4.793 \mathrm{E}-4$ | -0.2834 | -0.1803 | -0.07353 | 1001 | 10000 |
| sigma1 | 0.1106 | 0.03374 | $9.345 \mathrm{E}-4$ | 0.06492 | 0.1033 | 0.194 | 1001 | 10000 |
| sigma2 | 0.1399 | 0.05357 | 0.001464 | 0.04614 | 0.1355 | 0.2624 | 1001 | 10000 |
| theta | 0.993 | 0.05181 | $5.125 \mathrm{E}-4$ | 0.8934 | 0.9915 | 1.104 | 1001 | 10000 |

## Dyes: variance components model

Box and Tiao (1973) analyse data first presented by Davies (1967) concerning batch to batch variation in yields of dyestuff. The data (shown below) arise from a balanced experiment whereby the total product yield was determined for 5 samples from each of 6 randomly chosen batches of raw material.

| Batch | Yield (in grams) |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- |
| 1 | 1545 | 1440 | 1440 | 1520 | 1580 |
| 2 | 1540 | 1555 | 1490 | 1560 | 1495 |
| 3 | 1595 | 1550 | 1605 | 1510 | 1560 |
| 4 | 1445 | 1440 | 1595 | 1465 | 1545 |
| 5 | 1595 | 1630 | 1515 | 1635 | 1625 |
| 6 | 1520 | 1455 | 1450 | 1480 | 1445 |

The object of the study was to determine the relative importance of between batch variation versus variation due to sampling and analytic errors. On the assumption that the batches and samples vary independently, and contribute additively to the total error variance, we may assume the following model for dyestuff yield:

$$
\begin{aligned}
& y_{\mathrm{ij}} \sim \operatorname{Normal}\left(\mu_{\mathrm{i}}, \tau_{\text {within }}\right) \\
& \mu_{\mathrm{i}} \sim \operatorname{Normal}\left(\theta, \tau_{\text {between }}\right)
\end{aligned}
$$

where $y_{\mathrm{ij}}$ is the yield for sample $j$ of batch $i, \mu_{\mathrm{i}}$ is the true yield for batch $i, \tau_{\text {within }}$ is the inverse of the within-batch variance $\sigma^{2}$ within (i.e. the variation due to sampling and analytic error), $\theta$ is the true average yield for all batches and $\tau_{\text {between }}$ is the inverse of the between-batch variance $s^{2}$ between. The total variation in product yield is thus $\sigma^{2}$ total $=\sigma^{2}$ within $+\sigma^{2}$ between and the relative contributions of each component to the total variance are $f_{\text {within }}=\sigma^{2}{ }_{\text {within }} / \sigma_{\text {total }}$ and $f_{\text {between }}=$ $\sigma^{2}$ between $/ \sigma^{2}$ total . We assume standard non-informative priors for $\theta, \tau_{\text {within }}$ and $\tau_{\text {between }}$.


Bugs language for dyes example

```
model
{
    for(i in 1: batches) {
        m[i] ~ dnorm(theta, tau.btw)
        for(j in 1 : samples) {
            y[i ,j] ~ dnorm(m[i], tau.with)
        }
    }
    sigma2.with <-1 / tau.with
    sigma2.btw <- 1 / tau.btw
    tau.with ~ dgamma(0.001, 0.001)
    tau.btw ~ dgamma(0.001, 0.001)
    theta ~ dnorm(0.0, 1.0E-10)
}
```

Data (click to open)
Inits ( click to open)

## Results

A 25000 update burn in followed by a further 100000 updates gave the parameter estimates

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc | start | sample |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| sigma2.btw | 2207.0 | 4289.0 | 40.94 | 0.008042 | 1290.0 | 10210.0 | 25001 | 100000 |
| sigma2.with | 3034.0 | 1102.0 | 19.89 | 1561.0 | 2807.0 | 5752.0 | 25001 | 100000 |
| theta | 1528.0 | 21.5 | 0.1712 | 1484.0 | 1527.0 | 1571.0 | 25001 | 100000 |

Note that a relatively long run was required because of the high autocorrelation between successively sampled values of some parameters. Such correlations reduce the 'effective' size of the posterior sample, and hence a longer run is needed to ensure sufficient precision of the posterior estimates. Note that the posterior distribution for $\sigma^{2}$ between has a very long upper tail: hence the posterior mean is considerably larger than the median. Box and Tiao estimate $\sigma^{2}$ within $=2451$ and $\sigma^{2}$ between $=1764$ by classical analysis of variance. Here, $\sigma^{2}$ between is estimated by the difference of the between- and within-batch mean squares divided by the number of batches 1. In cases where the between-batch mean square within-batch mean square, this leads to the unsatisfactory situation of a negative variance estimate. Computing a confidence interval for $\sigma^{2}$ between is also difficult using the classical approach due to its complicated sampling distribution

BUGS

## Stacks: robust regression

Birkes and Dodge (1993) apply different regression models to the much-analysed stack-loss data of Brownlee (1965). This features 21 daily responses of stack loss $y$, the amount of ammonia escaping, with covariates being air flow $x_{1}$, temperature $x_{2}$ and acid concentration $x_{3}$. Part of the data is shown below.

| Day | Stack loss y | air flow $\mathrm{x}_{1}$ | temperature $\mathrm{x}_{2}$ | acid $\mathrm{x}_{3}$ |
| :--- | :--- | :--- | :--- | :--- |
| 1 | 42 | 80 | 27 | 89 |
| 2 | 37 | 80 | 27 | 88 |
| $\ldots \ldots$. |  |  |  |  |
| 21 | 15 | 70 | 20 | 91 |

We first assume a linear regression on the expectation of $y$, with a variety of different error structures. Specifically

$$
\begin{aligned}
& \mu_{i}=\beta_{0}+\beta_{1} z_{1 i}+\beta_{2} z_{2 i}+\beta_{3} z_{3 i} \\
& y_{i} \sim \operatorname{Normal}\left(\mu_{i}, \tau\right) \\
& y_{i} \sim \operatorname{Double} \exp \left(\mu_{i}, \tau\right) \\
& y_{i} \sim t\left(\mu_{i}, \tau, d\right)
\end{aligned}
$$

where $z_{\mathrm{ij}}=\left(\mathrm{x}_{\mathrm{ij}}-\mathrm{xbar} \mathrm{r}_{\mathrm{j}}\right) / \mathrm{sd}\left(\mathrm{x}_{\mathrm{j}}\right)$ are covariates standardised to have zero mean and unit variance. $\beta_{1}, \beta_{2}, \beta_{3}$ are initially given independent "noninformative" priors.

Maximum likelihood estimates for the double expontential (Laplace) distribution are essentially equivalent to minimising the sum of absolute deviations (LAD), while the other options are alternative heavy-tailed distributions. A t on 4 degrees of freedom has been chosen, although with more data it would be possible to allow this parameter also to be unknown.

We also consider the use of 'ridge regression', intended to avoid the instability due to correlated covariates. This has been shown Lindley and Smith (1972) to be equivalent to assuming the regression coefficients of the standardised covariates to be exchangeable, so that

$$
\beta_{\mathrm{j}} \sim \operatorname{Normal}(0, \phi), j=1,2,3 .
$$

In the following example we extend the work of Birkes and Dodge (1993) by applying this ridge
technique to each of the possible error distributions.
Birkes and Dodge (1993) suggest investigating outliers by examining residuals $y_{i}-\mu_{i}$ greater than 2.5 standard deviations. We can calculate standardised residuals for each of these distributions, and create a variable outlier[i] taking on the value 1 whenever this condition is fulfilled. Mean values of outlier[i] then show the confidence with which this definition of outlier is fulfilled.

The BUGS language for all the models is shown below, with all models except the normal linear regression commented out:

```
model
\{
\# Standardise x's and coefficients
    for (j in \(1: p\) ) \{
        b[j] <- beta[j] / sd(x[ , j])
        for (i in \(1: N\) ) \{
            \(z[i, j]<-(x[i, j]-\operatorname{mean}(x[, j])) / \operatorname{sd}(x[, j])\)
        \}
    \}
    \(\mathrm{b} 0<-\operatorname{beta0}-\mathrm{b}[1]{ }^{*}\) mean(x[, 1]) - b[2] * mean(x[, 2]) - b[3] * mean(x[, 3])
\# Model
    d <- 4; \# degrees of freedom for \(t\)
for (i in \(1: N\) ) \{
        Y[i] ~ dnorm(mu[i], tau)
\# \(\quad\) Y[i] ~ \(\operatorname{ddexp}(m u[i]\), tau \()\)
\# \(\quad \mathrm{Y}[\mathrm{i}] \sim \mathrm{dt}(\mathrm{mu}[\mathrm{i}]\), tau, d\()\)
        mu[i] <- beta0 + beta[1] * z[i, 1] + beta[2] * z[i, 2] + beta[3] * z[i, 3]
        stres[i] <- (Y[i] - mu[i]) / sigma
        outlier[i] <- step(stres[i] - 2.5) + step(-(stres[i] + 2.5) )
    \}
\# Priors
    beta0 ~ dnorm(0, 0.00001)
    for \((\mathrm{j}\) in \(1: p)\) \{
        beta[j] ~ dnorm(0, 0.00001) \# coeffs independent
\# beta[j] ~ dnorm(0, phi) \# coeffs exchangeable (ridge regression)
    \}
    tau ~ dgamma(1.0E-3, 1.0E-3)
    phi ~ dgamma(1.0E-2,1.0E-2)
\# standard deviation of error distribution
    sigma <- sqrt(1 / tau) \# normal errors
\# sigma <- sqrt(2) / tau \# double exponential errors
\# sigma <- sqrt(d / (tau * (d-2))); \#t errors on d degrees of freedom
\}
```

Data ( click to open)
Inits ( click to open )

## Results

## a) Normal error

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| b[1] | 0.7135 | 0.1402 | 0.002709 | 0.436 | 0.7129 | 0.9943 | 1001 | 10000 |
| $\mathrm{~b}[2]$ | 1.301 | 0.3829 | 0.007076 | 0.5377 | 1.3 | 2.053 | 1001 | 10000 |
| $\mathrm{~b}[3]$ | -0.1511 | 0.1666 | 0.00215 | -0.4792 | -0.1511 | 0.1836 | 1001 | 10000 |
| $\mathrm{b0}$ | -40.0 | 12.64 | 0.136 | -65.26 | -40.02 | -14.64 | 1001 | 10000 |
| outlier[3] | 0.01 | 0.0995 | $8.876 \mathrm{E}-4$ | 0.0 | 0.0 | 0.0 | 1001 | 10000 |
| outlier[4] | 0.0494 | 0.2167 | 0.002287 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[21] | 0.3118 | 0.4632 | 0.005947 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| sigma | 3.393 | 0.6217 | 0.007985 | 2.435 | 3.308 | 4.859 | 1001 | 10000 |

b) Double exponential error

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| b[1] | 0.831 | 0.131 | 0.003069 | 0.5563 | 0.8341 | 1.092 | 1001 | 10000 |
| b[2] | 0.7545 | 0.3405 | 0.007192 | 0.1691 | 0.7245 | 1.521 | 1001 | 10000 |
| b[3] | -0.1152 | 0.1199 | 0.001538 | -0.3629 | -0.1106 | 0.1157 | 1001 | 10000 |
| b0 | -38.78 | 8.788 | 0.08773 | -56.6 | -38.76 | -21.08 | 1001 | 10000 |
| outlier[1] | 0.0453 | 0.208 | 0.002081 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[3] | 0.0578 | 0.2334 | 0.002381 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[4] | 0.2929 | 0.4551 | 0.00534 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[21] | 0.59 | 0.4918 | 0.007638 | 0.0 | 1.0 | 1.0 | 1001 | 10000 |
| sigma | 3.492 | 0.8657 | 0.01174 | 2.169 | 3.362 | 5.528 | 1001 | 10000 |
| C) t4 error |  |  |  |  |  |  |  |  |

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| b[1] | 0.8361 | 0.1412 | 0.004002 | 0.5501 | 0.8401 | 1.114 | 1001 | 10000 |
| $\mathrm{~b}[2]$ | 0.8565 | 0.3744 | 0.01016 | 0.1622 | 0.8302 | 1.67 | 1001 | 10000 |
| $\mathrm{~b}[3]$ | -0.1254 | 0.1289 | 0.001917 | -0.3816 | -0.1251 | 0.1311 | 1001 | 10000 |
| b0 | -40.22 | 9.839 | 0.1218 | -59.98 | -40.16 | -20.85 | 1001 | 10000 |
| outlier[3] | 0.0334 | 0.1797 | 0.002467 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[4] | 0.2343 | 0.4236 | 0.007791 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[21] | 0.5904 | 0.4918 | 0.01125 | 0.0 | 1.0 | 1.0 | 1001 | 10000 |
| sigma | 3.478 | 0.8485 | 0.01899 | 2.146 | 3.368 | 5.464 | 1001 | 10000 |

## d) Normal eror ridge regression

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| b[1] | 0.6816 | 0.1345 | 0.002706 | 0.4144 | 0.6828 | 0.9451 | 1001 | 10000 |
| b[2] | 1.317 | 0.3652 | 0.006841 | 0.5829 | 1.318 | 2.042 | 1001 | 10000 |
| b[3] | -0.1266 | 0.1644 | 0.002001 | -0.4488 | -0.1267 | 0.2017 | 1001 | 10000 |
| b0 | -40.53 | 12.46 | 0.1255 | -65.46 | -40.51 | -15.94 | 1001 | 10000 |
| outlier[3] | 0.0189 | 0.1362 | 0.001325 | 0.0 | 0.0 | 0.0 | 1001 | 10000 |
| outlier[4] | 0.0471 | 0.2119 | 0.002388 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[21] | 0.2795 | 0.4488 | 0.006227 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| sigma | 3.395 | 0.6197 | 0.007177 | 2.425 | 3.312 | 4.828 | 1001 | 10000 |

## e) Double exponential error ridge regression

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc start | sample |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| b[1] | 0.796 | 0.1328 | 0.00319 | 0.5135 | 0.8005 | 1.058 | 1001 |
| b[2] | 0.7883 | 0.3334 | 0.007516 | 0.2109 | 0.7546 | 1.53 | 10000 |
| b[3] | -0.09911 | 0.1169 | 0.001705 | -0.3386 | -0.09686 | 0.1279 | 1001 |
| b0 | -38.82 | 8.665 | 0.09608 | -56.67 | -38.77 | -21.62 | 1001 |
| outlier[1] | 0.0603 | 0.238 | 0.00301 | 0.0 | 0.0 | 1.0 | 10000 |
| outlier[3] | 0.0735 | 0.261 | 0.00317 | 0.0 | 0.0 | 1.0 | 10000 |
| outlier[4] | 0.2875 | 0.4526 | 0.005526 | 0.0 | 0.0 | 1.0 | 1001 |
| outlier[21] | 0.5463 | 0.4979 | 0.008318 | 0.0 | 1.0 | 1.0 | 1001 |
| sigma | 3.499 | 0.8798 | 0.01195 | 2.17 | 3.359 | 5.636 | 1000 |
| sing | 10000 | 10000 |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| 10000 |  |  |  |  |  |  |  |

## f) t4 error ridge regression

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc start | sample |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| b[1] | 0.7949 | 0.1399 | 0.003333 | 0.5108 | 0.7975 | 1.063 | 1001 | 10000 |
| b[2] | 0.9094 | 0.3624 | 0.008192 | 0.2511 | 0.8879 | 1.701 | 1001 | 10000 |
| b[3] | -0.1087 | 0.1304 | 0.001715 | -0.3691 | -0.1071 | 0.1468 | 1001 | 10000 |
| b0 | -40.34 | 9.901 | 0.1074 | -60.01 | -40.33 | -20.52 | 1001 | 10000 |
| outlier[1] | 0.0327 | 0.1779 | 0.0023 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[3] | 0.0466 | 0.2108 | 0.002868 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[4] | 0.2127 | 0.4092 | 0.007202 | 0.0 | 0.0 | 1.0 | 1001 | 10000 |
| outlier[21] | 0.5218 | 0.4995 | 0.01065 | 0.0 | 1.0 | 1.0 | 1001 | 10000 |
| sigma | 3.521 | 0.8663 | 0.01802 | 2.157 | 3.41 | 5.487 | 1001 | 10000 |

We note the similar results between the Birkes and Dodge methods and BUGS, and the lack of influence of the ridge technique in this context.

## Blocker: random effects meta-analysis of clinical trials

Carlin (1992) considers a Bayesian approach to meta-analysis, and includes the following examples of 22 trials of beta-blockers to prevent mortality after myocardial infarction.

| Study | Mortality: deaths / total <br> Treated <br> Control |  |
| :--- | :--- | :--- |
| 1 | $3 / 38$ | $3 / 39$ |
| 2 | $7 / 114$ | $14 / 116$ |
| 3 | $5 / 69$ | $11 / 93$ |
| 4 | $102 / 1533$ | $127 / 1520$ |
| $\ldots$. |  |  |
| 20 | $32 / 209$ | $40 / 218$ |
| 21 | $27 / 391$ | $43 / 364$ |
| 22 | $22 / 680$ | $39 / 674$ |

In a random effects meta-analysis we assume the true effect (on a log-odds scale) $\delta_{i}$ in a trial $i$ is drawn from some population distribution. Let $\mathrm{r}_{\mathrm{i}}$ denote number of events in the control group in trial $i$, and $\mathrm{r}^{\top}{ }_{\mathrm{i}}$ denote events under active treatment in trial $i$. Our model is:

$$
\begin{aligned}
& \mathrm{r}_{\mathrm{i}} \sim \operatorname{Binomial}\left(\mathrm{p}_{\mathrm{i}}, \mathrm{n}_{\mathrm{i}}\right) \\
& \mathrm{r}_{\mathrm{i}}{ }_{\mathrm{T}} \sim \operatorname{Binomial}\left(\mathrm{p}_{\mathrm{i}}, \mathrm{n}_{\mathrm{i}}{ }^{2}\right) \\
& \operatorname{logit}\left(\mathrm{p} \mathrm{C}_{\mathrm{i}}\right)=\mu_{\mathrm{i}} \\
& \operatorname{logit}\left(\mathrm{p}_{\mathrm{i}}{ }_{\mathrm{i}}\right)=\mu_{\mathrm{i}}+\delta_{\mathrm{i}} \\
& \delta_{\mathrm{i}} \sim \operatorname{Normal}(\mathrm{~d}, \tau)
\end{aligned}
$$

"Noninformative" priors are given for the $\mu_{\mathrm{j}} \mathrm{s}$. $\tau$ and d. The graph for this model is shown in below. We want to make inferences about the population effect d , and the predictive distribution for the effect $\delta_{\text {new }}$ in a new trial. Empirical Bayes methods estimate d and $\tau$ by maximum likelihood and use these estimates to form the predictive distribution $\mathrm{p}\left(\delta_{\text {new }} \mid \mathrm{d}_{\text {hat }}, \tau_{\text {hat }}\right)$. Full Bayes allows for the uncertainty concerning d and $\tau$.


BUGS language for blocker example:

```
model
{
    for(i in 1:Num ) {
        rc[i] ~ dbin(pc[i], nc[i])
        rt[i] ~ dbin(pt[i], nt[i])
        logit(pc[i]) <- mu[i]
        logit(pt[i]) <- mu[i] + delta[i]
        mu[i] ~ dnorm(0.0,1.0E-5)
        delta[i] ~ dt(d, tau, 4)
    }
    d ~ dnorm(0.0,1.0E-6)
    tau ~ dgamma(0.001,0.001)
    delta.new ~ dt(d, tau, 4)
    sigma <-1 / sqrt(tau)
}
```

Data (click to open)
Inits (click to open)
Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc start | sample |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| d | -0.2492 | 0.06422 | 0.002004 | -0.3727 | -0.2502 | -0.1194 | 1001 |
| delta.new | -0.2499 | 0.1509 | 0.002389 | -0.5592 | -0.2536 | 0.07169 | 1001 |
| sigma | 0.1189 | 0.07 | 0.003521 | 0.02428 | 0.1067 | 0.2825 | 1001 |

Our estimates are lower and with tighter precision - in fact similar to the values obtained by Carlin for the empirical Bayes estimator. The discrepancy appears to be due to Carlin's use of a uniform prior for $\sigma^{2}$ in his analysis, which will lead to increased posterior mean and standard deviation for $d$, as compared to our (approximate) use of $p\left(\sigma^{2}\right) \sim 1 / \sigma^{2}$ (see his Figure 1).

In some circumstances it might be reasonable to assume that the population distribution has heavier tails, for example a t distribution with low degrees of freedom. This is easily accomplished in BUGS by using the dt distribution function instead of dnorm for $\delta$ and $\delta_{\text {new }}$.

## Oxford: smooth fit to log-odds ratios

Breslow and Clayton (1993) re-analyse 2 by 2 tables of cases (deaths from childhood cancer) and controls tabulated against maternal exposure to X-rays, one table for each of 120 combinations of age (0-9) and birth year (1944-1964). The data may be arranged to the following form.

| Strata | Exposure: X-ray / total <br> Cases |  | age | year-1954 |
| :--- | :--- | :--- | :--- | :--- |
|  |  | $0 / 28$ | 9 | -10 |
| 1 | $3 / 28$ |  |  |  |
| 120 | $7 / 32$ | $1 / 32$ | 1 | 10 |

Their most complex model is equivalent to expressing the $\log$ (odds-ratio) $\psi_{i}$ for the table in stratum $i$ as

$$
\begin{aligned}
& \log \psi_{i}=\alpha+\beta_{1} \text { year }_{i}+\beta_{2}\left(\text { year }_{i}^{2}-22\right)+b_{i} \\
& b_{i} \sim \operatorname{Normal}(0, \tau)
\end{aligned}
$$

They use a quasi-likelihood approximation of the full hypergeometric likelihood obtained by conditioning on the margins of the tables.

We let $r_{i}$ denote number of exposures among the $\mathrm{n}_{\mathrm{i}}$ controls in stratum $i$, and $r^{1}{ }_{i}$ denote number of exposures for the $\mathrm{n}^{1}{ }_{i}$ cases. The we assume

$$
\begin{aligned}
& r_{i}^{0} \sim \operatorname{Binomial}\left(p_{i}^{0}, n_{i}^{0}\right) \\
& r_{i}^{1} \sim \operatorname{Binomial}\left(p^{1}, n_{i}^{1}\right) \\
& \operatorname{logit}\left(p_{i} 0_{i}\right)=\mu_{i} \\
& \operatorname{logit}\left(p_{i}^{1}\right)=\mu_{i}+\log \psi_{i}
\end{aligned}
$$

Assuming this model with independent vague priors for the $\mu_{\mathrm{i}}$ 's provides the correct conditional likelihood. The appropriate graph is shown below


## BUGS language for Oxford example:

```
model
\{
    for (i in \(1: K\) ) \{
        \(\mathrm{rO}[\mathrm{i}] \sim \operatorname{dbin}(\mathrm{pO}[\mathrm{i}], \mathrm{nO}[\mathrm{i}])\)
        r1[i] ~ dbin(p1[i], n1[i])
        \(\operatorname{logit}(p 0[i])<-m u[i]\)
        \(\operatorname{logit}(p 1[i])<-\) mu[i] \(+\log P s i[i]\)
        logPsi[i] <- alpha + beta1 * year[i] + beta2 * (year[i] * year[i] - 22) + b[i]
        b[i] ~ dnorm(0, tau)
        mu[i] ~ dnorm(0.0, 1.0E-6)
    \}
    alpha ~ dnorm(0.0, 1.0E-6)
    beta1 ~ dnorm(0.0, 1.0E-6)
    beta2 ~ dnorm(0.0, 1.0E-6)
    tau ~dgamma(1.0E-3, 1.0E-3)
    sigma <-1 / sqrt(tau)
\}
```


## Data ( click to open )

Inits ( click to open)

## Examples Volume I

Oxford

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc | start | sample |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| alpha | 0.579 | 0.062 | 0.001545 | 0.4587 | 0.5793 | 0.7037 | 1001 |
| beta1 | -0.04557 | 0.01553 | $3.929 \mathrm{E}-4$ | -0.07688 | -0.0457 | -0.01586 | 1001 |
| beta2 | 0.007041 | 0.003084 | $8.953 \mathrm{E}-5$ | 0.001018 | 0.007004 | 0.01314 | 1001 |
| sigma | 0.09697 | 0.06011 | 0.005036 | 0.02419 | 0.08059 | 0.2457 | 1001 |

These estimates compare well with Breslow and Clayton (1993) PQL estimates of $\alpha=0.566+/-$ $0.070, \beta_{1}=-0.469+/-0.0167, \beta_{2}=0.0071+/-0.0033, \sigma=0.15+/-0.10$.

## LSAT: item response

Section 6 of the Law School Aptitude Test (LSAT) is a 5-item multiple choice test; students score 1 on each item for the correct answer and 0 otherwise, giving $R=32$ possible response patterns.Boch and Lieberman (1970) present data on LSAT for $\mathrm{N}=1000$ students, part of which is shown below.

| Pattern index | Item response pattern | Freq (m) |
| :---: | :---: | :---: |
| 1 | 00000 | 3 |
| 2 | 00001 | 6 |
| 3 | 00010 | 2 |
| . | . . . . |  |
|  |  |  |
| 30 | 11101 | 61 |
| 31 | 11110 | 28 |
| 32 | 11111 | 298 |

The above data may be analysed using the one-parameter Rasch model (see Andersen (1980), pp.253-254; Boch and Aitkin (1981)). The probability $\mathrm{p}_{\mathrm{jk}}$ that student $j$ responds correctly to item $k$ is assumed to follow a logistic function parameterized by an 'item difficulty' or threshold parameter $\alpha_{k}$ and a latent variable $\theta_{j}$ representing the student's underlying ability. The ability parameters are assumed to have a Normal distribution in the population of students. That is:

$$
\begin{aligned}
& \operatorname{logit}\left(p_{j k}\right)=\theta_{j}-\alpha_{k}, j=1, \ldots, 1000 ; k=1, \ldots, 5 \\
& \theta_{j} \sim \operatorname{Normal}(0, \tau)
\end{aligned}
$$

The above model is equivalent to the following random effects logistic regression:

$$
\begin{aligned}
& \operatorname{logit}\left(p_{j k}\right)=\beta \theta_{j}-\alpha_{k}, j=1, \ldots, 1000 ; k=1, \ldots, 5 \\
& \theta_{\mathrm{j}} \sim \operatorname{Normal}(0,1)
\end{aligned}
$$

where $\beta$ corresponds to the scale parameter $\left(\beta^{2}=\tau\right)$ of the latent ability distribution. We assume a half-normal distribution with small precision for $\beta$; this represents vague prior information but constrains $\beta$ to be positive. Standard vague normal priors are assumed for the $\alpha_{k}$ 's. Note that the location of the $\alpha_{k}$ 's depend upon the mean of the prior distribution for $\theta_{j}$ which we have
arbitrarily fixed to be zero. Alternatively, Boch and Aitkin ensure identifiability by imposing a sum-to-zero constraint on the $\alpha_{k}$ 's. Hence we calculate $a_{k}=\alpha_{k}-\alpha_{b a r}$ to enable comparision of the BUGS posterior parameter estimates with the Boch and Aitkin marginal maximum likelihood estimates.

## BUGS language for LSAT model

```
model
{
# Calculate individual (binary) responses to each test from multinomial data
    for (j in 1 : culm[1]) {
        for (k in 1:T) {
            r[j, k] <- response[1, k]
        }
    }
    for (i in 2: R) {
        for (j in culm[i-1] + 1 : culm[i]) {
            for (k in 1:T) {
                r[j, k] <- response[i, k]
            }
        }
    }
# Rasch model
    for (j in 1:N) {
        for (k in 1:T) {
            logit(p[j, k]) <- beta * theta[j] - alpha[k]
            r[j, k] ~ dbern(p[j, k])
        }
        theta[j] ~ dnorm(0, 1)
    }
# Priors
    for (k in 1:T) {
        alpha[k] ~ dnorm(0, 0.0001)
        a[k] <- alpha[k] - mean(alpha[])
    }
    beta ~ dnorm(0,0.0001)I(0, )
}
```

Note that the data are read into BUGS in the original multinomial format to economize on space and effort. The 5 times 1000 individual binary responses for each item and student are then created within BUGS using the index variable culm (read in from the data file), where culm[i] = cumulative number of students recording response patterns $1,2, \ldots, i ; i<=R$.

## Data (click to open )

## Inits ( click to open )

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| $\mathrm{a}[1]$ | -1.261 | 0.1048 | 0.001383 | -1.468 | -1.258 | -1.06 | 1001 | 10000 |
| $\mathrm{a}[2]$ | 0.4788 | 0.07014 | $7.807 \mathrm{E}-4$ | 0.3419 | 0.4787 | 0.62 | 1001 | 10000 |
| $\mathrm{a}[3]$ | 1.238 | 0.07017 | $9.431 \mathrm{E}-4$ | 1.102 | 1.237 | 1.376 | 1001 | 10000 |
| $\mathrm{a}[4]$ | 0.1697 | 0.0731 | $8.377 \mathrm{E}-4$ | 0.02005 | 0.1718 | 0.3104 | 1001 | 10000 |
| $\mathrm{a}[5]$ | -0.6257 | 0.08552 | 0.001034 | -0.7943 | -0.6242 | -0.4612 | 1001 | 10000 |
| beta | 0.7581 | 0.06914 | 0.001899 | 0.6223 | 0.7576 | 0.8957 | 1001 | 10000 |

## Bones: latent trait model for multiple ordered catagorical responses

The concept of skeletal age (SA) arises from the idea that individuals mature at different rates: for any given chronological age (CA), the average SA in a sample of individuals should equal their CA, but with an inter-individual spread which reflects the differential rate of maturation. Roche et al (1975) have developed a model for predicting SA by calibrating 34 indicators (items) of skeletal maturity which may be observed in a radiograph. Each indicator is categorized with respect to its degree of maturity: 19 are binary items (i.e. $0=$ immature or $1=$ mature); 8 items have 3 grades (i.e. $0=$ immature; $1=$ partially mature; 2 = fully mature); 1 item has 4 ordered grades and the remaining 6 items have 5 ordered grades of maturity. Roche et al. calculated threshold parameters for the boundarys between grades for each indicator. For the binary items, there is a single threshold representing the CA at which $50 \%$ of individuals are mature for the indicator. Three-category items have 2 threshold parameters: the first corresponds to the CA at which $50 \%$ of individuals are either partially or fully mature for the indicator; the second is the CA at which $50 \%$ of individuals are fully mature. Four and five-category items have 3 and 4 threshold parameters respectively, which are interpreted in a similar manner to those for 3 -category items. In addition, Roche et al. calculated a discriminability (slope) parameter for each item which reflects its rate of maturation. Part of this data is shown below. Columns 1--4 represent the threshold parameters (note the use of the missing value code NA to 'fill in' the columns for items with fewer than 4 thresholds); column 5 is the discriminability parameter; column 6 gives the number of grades per item.

| Threshold parameters |  |  |  | Discriminability | Num grades |
| :--- | :--- | :--- | :--- | :--- | :--- |
| 0.7425 | NA | NA | NA | 2.9541 | 2 |
| 10.2670 | NA | NA | NA | 0.6603 | 2 |
| 10.5215 | NA | NA | NA | 0.7965 | 2 |
| 9.3877 | NA | NA | NA | 1.0495 | 2 |
| 0.2593 | NA | NA | NA | 5.7874 | 2 |
| $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ |
| . | $\cdot$ | $\cdot$ | . | . | $\cdot$ |
| 0.3887 | 1.0153 | NA | NA | 8.1123 | 3 |
| 3.2573 | 7.0421 | NA | NA | 0.9974 | 3 |
| $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ |
| $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ |
| 15.4750 | 16.9406 | 17.4944 | NA | 1.4297 | 4 |
| $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ |
| $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ | $\cdot$ |
| 5.0022 | 6.3704 | 8.2832 | 10.4988 | 1.0954 | 5 |
| 4.0168 | 5.1537 | 7.1053 | 10.3038 | 1.5329 | 5 |

Thissen (1986) (p.71) presents the following graded radiograph data on 13 boys whose
chronological ages range from 6 months to 18 years. (Note that for ease of implementation in $B U G S$ we have listed the items in a different order to that used by Thissen):


Some items have missing data (represented by the code NA in the table above). This does not present a problem for BUGS: the missing grades are simply treated as unknown parameters to be estimated along with the other parameters of interest such as the SA for each boy.

Thissen models the above data using the logistic function. For each item $j$ and each grade $k$, the cumulative probability $\mathrm{Q}_{\mathrm{jk}}$ that a boy with skeletal age $\theta$ is assigned a more mature grade than $k$ is given by

$$
\operatorname{logit}_{\mathrm{jk}}=\delta_{\mathrm{j}}\left(\theta-\gamma_{\mathrm{jk}}\right)
$$

where $\delta_{\mathrm{j}}$ is the discriminability parameter and the $\gamma_{\mathrm{jk}}$ are the threshold parameters for item $j$. Hence the probability of observing an immature grade (i.e. $\mathrm{k}=1$ ) for a particular skeletal age $\theta$ is $\mathrm{p}_{\mathrm{j}, 1}=1-\mathrm{Q}_{\mathrm{j}, 1}$. The probability of observing a fully mature grade (i.e. $\mathrm{k}=\mathrm{K}_{\mathrm{j}}$, where $\mathrm{K}_{\mathrm{j}}$ is the number of grades for item $j$ is $\mathrm{p}_{\mathrm{j},}, \mathrm{K}_{\mathrm{j}}=\mathrm{Q}_{\mathrm{j},}, \mathrm{K}_{\mathrm{j}-1}$. For items with 3 or more categories, the probability of observing an itermediate grade is $\mathrm{p}_{\mathrm{j}, \mathrm{k}}=\mathrm{Q}_{\mathrm{j}, \mathrm{k}-1}-\mathrm{Q}_{\mathrm{j}, \mathrm{k}}$ (i.e. the difference between the cumulative probability of being assigned grade $k$ or more, and of being assigned grade $k+1$ or more).

The BUGS language for this model is given below. Note that the $\theta_{i}$ for each boy $i$ is assigned a vague, independent normal prior theta[i] ~ dnorm( $0.0,0.001$ ). That is, each boy is treated as a separate problem with is no `learning' or 'borrowing strength' across individuals, and hence no hierachical structure on the $\theta_{j}$ 's.

## BUGS language for bones example

```
model
{
    for (i in 1: nChild) {
        theta[i] ~ dnorm(0.0, 0.001)
        for (j in 1: nlnd) {
# Cumulative probability of > grade k given theta
        for (k in 1: ncat[j] - 1) {
            logit(Q[i, j, k]) <- delta[j] * (theta[i] - gamma[j, k])
```

```
            }
        }
# Probability of observing grade k given theta
    for (j in 1: nlnd) {
        p[i, j, 1] <- 1- Q[i, j, 1]
        for (k in 2 : ncat[j] - 1) {
                p[i, j, k] <- Q[i, j, k - 1] - Q[i, j, k]
            }
            p[i, j, ncat[j]] <- Q[i, j, ncat[j] - 1]
            grade[i, j] ~ dcat(p[i, j, 1 : ncat[j]])
        }
    }
}
```


## Data ( click to open )

Inits ( click to open )

We note a couple of tricks used in the above code. Firstly, the variable $p$ has been declared as a 3-way rectangular array with the size of the third dimension equal to the maximum number of possible grades (i.e.5) for all items (even though items 1--28 have fewer than 5 categories). The statement

$$
\text { grade[i, j] ~ dcat(p[i, j, } 1 \text { :ngrade[j]]) }
$$

is then used to select the relevant elements of $p[i, j$, ] for item $j$, thus ignoring any `empty' spaces in the array for items with fewer than the maximum number of grades. Secondly, the final section of the above code includes a loop indexed as follows

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc start | sample |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| theta[1] | 0.3244 | 0.2085 | 0.002304 | -0.0999 | 0.3317 | 0.7238 | 1001 | 10000 |
| theta[2] | 1.366 | 0.256 | 0.002403 | 0.8998 | 1.352 | 1.899 | 1001 | 10000 |
| theta[3] | 2.357 | 0.2726 | 0.002822 | 1.823 | 2.355 | 2.903 | 1001 | 10000 |
| theta[4] | 2.902 | 0.2959 | 0.002816 | 2.317 | 2.901 | 3.476 | 1001 | 10000 |
| theta[5] | 5.535 | 0.4996 | 0.004758 | 4.599 | 5.527 | 6.542 | 1001 | 10000 |
| theta[6] | 6.751 | 0.6046 | 0.006357 | 5.597 | 6.741 | 7.951 | 1001 | 10000 |
| theta[7] | 6.451 | 0.5857 | 0.005726 | 5.358 | 6.431 | 7.638 | 1001 | 10000 |
| theta[8] | 8.93 | 0.6971 | 0.006642 | 7.546 | 8.938 | 10.3 | 1001 | 10000 |
| theta[9] | 8.981 | 0.6719 | 0.007133 | 7.629 | 8.993 | 10.27 | 1001 | 10000 |
| theta[10] | 11.94 | 0.6871 | 0.00698 | 10.63 | 11.93 | 13.28 | 1001 | 10000 |
| theta[11] | 11.58 | 0.9078 | 0.009463 | 9.957 | 11.53 | 13.48 | 1001 | 10000 |
| theta[12] | 15.79 | 0.5624 | 0.005932 | 14.72 | 15.79 | 16.92 | 1001 | 10000 |
| theta[13] | 16.96 | 0.7477 | 0.007337 | 15.56 | 16.93 | 18.52 | 1001 | 10000 |

## Inhaler: ordered catagorical data

Ezzet and Whitehead (1993) analyse data from a two-treatment, two-period crossover trial to compare 2 inhalation devices for delivering the drug salbutamol in 286 asthma patients. Patients were asked to rate the clarity of leaflet instructions accompanying each device, using a 4-point ordinal scale. In the table below, the first entry in each cell $(r, c)$ gives the number of subjects in Group 1 (who received device $A$ in period 1 and device $B$ in period 2) giving response $r$ in period 1 and response c in period 2. The entry in brackets is the number of Group 2 subjects (who received the devices in reverse order) giving this response pattern.

|  | $\begin{gathered} 1 \\ \text { Easy } \end{gathered}$ | Response in 2 <br> Only clear after re-reading | period 2 <br> 3 <br> Not very clear | 4 Confusing | TOTAL |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Response | 59 (63) | 35 (13) | 3 (0) | 2 (0) | 99 (76) |
| in 2 | 11 (40) | 27 (15) | 2 (0) | 1 (0) | 41 (55) |
| period 13 | 0 (7) | 0 (2) | 0 (1) | 0 (0) | 0 (10) |
| 4 | 1 (2) | 1 (0) | 0 (1) | 0 (0) | 2 (3) |
| TOTAL | 71 (112) | 63 (30) | 5 (2) | 3 (0) | 142 (144) |

The response $\mathrm{R}_{\mathrm{it}}$ from the $i$ th subject $(i=1, \ldots, 286)$ in the $t$ th period $(t=1,2)$ thus assumes integer values between 1 and 4. It may be expressed in terms of a continuous latent variable $Y_{\text {it }}$ taking values on (-inf, inf) as follows:

$$
R_{i t}=j \text { if } Y_{i t} \text { in }\left[a_{j-1}, a_{j}\right), \quad j=1, . ., 4
$$

where $a_{0}=-\inf$ and $a_{4}=$ inf. Assuming a logistic distribution with mean $\mu_{i t}$ for $Y_{i t}$, then the cumulative probability $\mathrm{Q}_{\mathrm{itj}}$ of subject $i$ rating the treatment in period $t$ as worse than category $j$ (i.e. $\operatorname{Prob}\left(Y_{i t}>=a_{j}\right)$ is given by

$$
\operatorname{logitQ} Q_{i t j}=-\left(a j+\mu_{s_{i}} t+b_{i}\right)
$$

where $\mathrm{b}_{\mathrm{i}}$ represents the random effect for subject $i$. Here, $\mu_{\mathrm{s} j}$ depends only on the period $t$ and the sequence $\mathrm{s}_{\mathrm{i}}=1,2$ to which patient $i$ belongs. It is defined as

$$
\mu_{11}=\beta / 2+\pi / 2
$$

$$
\begin{aligned}
& \mu_{12}=-\beta / 2-\pi / 2-\kappa \\
& \mu_{21}=-\beta / 2+\pi / 2 \\
& \mu_{22}=\beta / 2-\pi / 2+\kappa
\end{aligned}
$$

where $\beta$ represents the treatment effect, $\pi$ represents the period effect and $\kappa$ represents the carryover effect. The probability of subject $i$ giving response $j$ in period $t$ is thus given by $\mathrm{p}_{\mathrm{itj}}=\mathrm{Q}_{\mathrm{itj}}$ $-1-Q_{i t}$, where $Q_{i t 0}=1$ and $Q_{i t 4}=0$ (see also the Bones example).

The BUGS language for this model is shown below. We assume the $\mathrm{b}_{;}$'s to be normally distributed with zero mean and common precision $\tau$. The fixed effects $\beta, \pi$ and $\kappa$ are given vague normal priors, as are the unknown cut points $\mathrm{a}_{1}, \mathrm{a}_{2}$ and $\mathrm{a}_{3}$. We also impose order constraints on the latter using the $I($,$) notation in BUGS, to ensure that \mathrm{a}_{1}<\mathrm{a}_{2}<\mathrm{a}_{3}$.

```
model
{
#
# Construct individual response data from contingency table
#
    for (i in 1: Ncum[1, 1]) {
        group[i] <- 1
        for (t in 1:T) { response[i, t] <- pattern[1, t] }
    }
    for (i in (Ncum[1,1] + 1) : Ncum[1, 2]) {
        group[i] <- 2 for (t in 1:T) {response[i, t] <- pattern[1, t] }
    }
    for (k in 2 : Npattern) {
        for(i in (Ncum[k - 1, 2] + 1) : Ncum[k, 1]) {
            group[i] <- 1 for (t in 1:T) { response[i, t] <- pattern[k, t] }
        }
        for(i in (Ncum[k, 1] + 1) : Ncum[k, 2]) {
            group[i] <- 2 for (t in 1:T) { response[i, t] <- pattern[k, t] }
        }
    }
#
# Model
#
    for (i in 1:N) {
        for (t in 1:T) {
            for (j in 1:Ncut) {
#
# Cumulative probability of worse response than j
#
```

```
            logit(Q[i, t, j]) <- -(a[j] + mu[group[i], t] + b[i])
        }
#
# Probability of response = j
#
    p[i, t, 1] <- 1- Q[i, t, 1]
    for (j in 2 : Ncut) { p[i, t, j] <- Q[i, t, j - 1] - Q[i, t, j] }
    p[i, t, (Ncut+1)] <- Q[i, t, Ncut]
            response[i, t] ~ dcat(p[i, t, ])
    }
#
# Subject (random) effects
#
    b[i] ~ dnorm(0.0, tau)
}
#
# Fixed effects
#
    for (g in 1 : G) {
        for(t in 1:T) {
# logistic mean for group i in period t
            mu[g, t] <- beta * treat[g, t] / 2 + pi * period[g, t] / 2 + kappa * carry[g, t]
        }
    }
    beta ~ dnorm(0, 1.0E-06)
    pi ~ dnorm(0, 1.0E-06)
    kappa ~ dnorm(0, 1.0E-06)
# ordered cut points for underlying continuous latent variable
    a[1] ~ dnorm(0, 1.0E-06)I(, a[2])
    a[2] ~ dnorm(0, 1.0E-06)!(a[1], a[3])
    a[3] ~ dnorm(0, 1.0E-06)l(a[2], )
    tau ~ dgamma(0.001, 0.001)
    sigma <- sqrt(1 / tau)
    log.sigma <- log(sigma)
}
```

Note that the data is read into BUGS in the original contigency table format to economize on space and effort. The indivdual responses for each of the 286 patients are then constructed within BUGS.

Data (click to open)

Inits ( click to open)

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| $\mathrm{a}[1]$ | 0.712 | 0.1382 | 0.004156 | 0.4566 | 0.7069 | 0.9981 | 1001 | 10000 |
| $\mathrm{a}[2]$ | 3.936 | 0.3298 | 0.01597 | 3.326 | 3.924 | 4.614 | 1001 | 10000 |
| $\mathrm{a}[3]$ | 5.28 | 0.4699 | 0.01893 | 4.412 | 5.262 | 6.239 | 1001 | 10000 |
| beta | 1.067 | 0.3199 | 0.008454 | 0.4575 | 1.057 | 1.714 | 1001 | 10000 |
| kappa | 0.2463 | 0.2503 | 0.005605 | -0.2394 | 0.2456 | 0.7475 | 1001 | 10000 |
| log.sigma | 0.195 | 0.203 | 0.01356 | -0.2494 | 0.2145 | 0.5424 | 1001 | 10000 |
| pi | -0.2367 | 0.1976 | 0.002313 | -0.6214 | -0.238 | 0.1509 | 1001 | 10000 |
| sigma | 1.24 | 0.2412 | 0.01562 | 0.7793 | 1.239 | 1.72 | 1001 | 10000 |

The estimates can be compared with those of Ezzet and Whitehead, who used the NewtonRaphson method and numerical integration to obtain maximum-likelihood estimates of the parameters. They reported $\beta=1.17+/-0.75, \pi=-0.23+/-0.20, \kappa=0.21+/-0.49$, $\log \sigma=0.17+/-$ $0.23, \mathrm{a} 1=0.68, \mathrm{a} 2=3.85, \mathrm{a} 3=5.10$

## Mice: Weibull regression

Dellaportas and Smith (1993) analyse data from Grieve (1987) on photocarcinogenicity in four groups, each containing 20 mice, who have recorded a survival time and whether they died or were censored at that time. A portion of the data, giving survival times in weeks, are shown below. A * indicates censoring.

| Mouse | Irradiated <br> control | Vehicle <br> control | Test <br> substance | Positive <br> control |
| :--- | :--- | :--- | :--- | :--- |
| 1 | 12 | 32 | 22 | 27 |
| $\ldots \ldots$. |  |  |  |  |
| 18 | $* 40$ | 30 | 24 | 12 |
| 19 | 31 | 37 | 37 | 17 |
| 20 | 36 | 27 | 29 | 26 |

The survival distribution is assumed to be Weibull. That is

$$
\mathrm{f}\left(\mathrm{t}_{\mathrm{i}}, \mathbf{z}_{\mathrm{i}}\right)=\mathrm{re} \beta \mathbf{z}_{\mathrm{i}} \mathrm{t}_{\mathrm{i}}^{\mathrm{r}}-1 \exp \left(-\mathrm{e}^{\beta} \mathbf{z}_{\mathrm{i} \mathrm{i}^{\mathrm{r}}} \mathrm{t}^{r}\right)
$$

where $t_{j}$ is the failure time of an individual with covariate vector $\mathbf{z}_{i}$ and $\beta$ is a vector of unknown regression coefficients. This leads to a baseline hazard function of the form

$$
\lambda_{0}\left(\mathrm{t}_{\mathrm{i}}\right)=\mathrm{rt}_{\mathrm{i}}{ }^{\mathrm{r}-1}
$$

Setting $\mu_{i}=e^{\beta \mathbf{z}_{i}}$ gives the parameterisation

$$
\mathrm{t}_{\mathrm{i}} \sim \text { Weibull }\left(\tau, \mu_{\mathrm{i}}\right)
$$

For censored observations, the survival distribution is a truncated Weibull, with lower bound corresponding to the censoring time. The regression $\beta$ coefficients were assumed a priori to follow independent Normal distributions with zero mean and "vague" precision 0.0001. The shape parameter $r$ for the survival distribution was given a Gamma(1, 0.0001) prior, which is slowly decreasing on the positive real line.

Median survival for individuals with covariate vector $\mathbf{z}_{i}$ is given by $m_{i}=\left(\log 2 e^{-\beta} \mathbf{z}_{i}\right)^{1 / r}$
The appropriate graph and BUGS language are below, using an undirected dashed line to represent a logical range constraint.


```
model
{
    for(i in 1:M) {
        for(j in 1:N) {
            t[i, j] ~ dweib(r, mu[i])(t.cen[i, j],)
        }
        mu[i] <- exp(beta[i])
        beta[i] ~ dnorm(0.0, 0.001)
        median[i] <- pow(log(2) * exp(-beta[i]), 1/r)
    }
    r ~ dexp(0.001)
    veh.control <- beta[2] - beta[1]
    test.sub <- beta[3] - beta[1]
    pos.control <- beta[4] - beta[1]
}
```

We note a number of tricks in setting up this model. First, individuals who are censored are given a missing value in the vector of failure times $t$, whilst individuals who fail are given a zero in the censoring time vector t.cen (see data file listing below). The truncated Weibull is modelled using $\mathrm{l}(\mathrm{t}$.cen[ $[\mathrm{i}$, ) to set a lower bound. Second, we set a parameter beta[j] for each treatment group $j$. The contrasts beta[j] with group 1 (the irradiated control) are calculated at the end. Alternatively, we could have included a grand mean term in the relative risk model and constrained beta[1] to be zero.

## Examples Volume I

Mice

## Data ( click to open )

## Inits ( click to open)

## Results

A burn in of 1000 updates followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc | median | val97.5pc start | sample |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| median[1] | 23.65 | 2.002 | 0.05203 | 20.06 | 23.54 | 27.93 | 1001 | 10000 |
| median[2] | 35.18 | 3.54 | 0.05764 | 29.22 | 34.88 | 43.21 | 1001 | 10000 |
| median[3] | 26.68 | 2.437 | 0.05828 | 22.36 | 26.5 | 31.99 | 1001 | 10000 |
| median[4] | 21.28 | 1.849 | 0.03371 | 18.01 | 21.16 | 25.36 | 1001 | 10000 |
| pos.control | 0.3088 | 0.3416 | 0.005912 | -0.3644 | 0.3115 | 0.9685 | 1001 | 10000 |
| r | 2.902 | 0.2781 | 0.02332 | 2.367 | 2.904 | 3.444 | 1001 | 10000 |
| test.sub | -0.3475 | 0.3435 | 0.004663 | -1.022 | -0.3478 | 0.3185 | 1001 | 10000 |
| veh.control | -1.143 | 0.365 | 0.006778 | -1.87 | -1.141 | -0.4315 | 1001 | 10000 |

bugs

## Kidney: Weibull regression with random efects

McGilchrist and Aisbett (1991) analyse time to first and second recurrence of infection in kidney patients on dialysis using a Cox model with a multiplicative frailty parameter for each individual. The risk variables considered are age, sex and underlying disease (coded other, GN, AN and PKD). A portion of the data are shown below.

| Patient <br> Number | Recurrence <br> time $t$ | Event <br> $(2=$ cens $)$ | Age at <br> time $t$ | Sex <br> $(1=$ female $)$ | Disease <br> $(0=$ other; $1=\mathrm{GN}$ <br> $2=$ AN; $3=$ PKD $)$ |
| :--- | :--- | :--- | :--- | :--- | :--- |
| 1 | 8,16 | 1,1 | 28,28 | 0 | 0 |
| 2 | 23,13 | 1,2 | 48,48 | 1 | 1 |
| 3 | 22,28 | 1,1 | 32,32 | 0 | 0 |
| 4 | 447,318 | 1,1 | 31,32 | 1 | 0 |
| $\ldots$. |  |  |  |  |  |
| 35 | 119,8 | 1,1 | 22,22 | 1 | 1 |
| 36 | 54,16 | 2,2 | 42,42 | 1 | 1 |
| 37 | 6,78 | 2,1 | 52,52 | 1 | 3 |
| 38 | 63,8 | 1,2 | 60,60 | 0 | 3 |

We have analysed the same data assuming a parametric Weibull distribution for the survivor function, and including an additive random effect $b_{i}$ for each patient in the exponent of the hazard model as follows

$$
\begin{aligned}
\mathrm{t}_{\mathrm{ij}} \sim & \text { Weibull }\left(\mathrm{r}, \mu_{\mathrm{ij}}\right) \quad \mathrm{i}=1, \ldots, 38 ; j=1,2 \\
\log _{\mathrm{ij}}= & \alpha+\beta_{\text {age }} \text { AGE }_{\mathrm{ij}}+\beta_{\text {sex }} \text { SEX }_{i}+\beta_{\text {disease1 }} \text { DISEASE }_{\mathrm{i} 1}+ \\
& \beta_{\text {disease2 }} \text { DISEASE }_{\mathrm{i} 2}+\beta_{\text {disease3 }} \text { DISEASE }_{i 3}+b_{i}
\end{aligned}
$$

$$
\mathrm{b}_{\mathrm{i}} \sim \operatorname{Normal}(0, \tau)
$$

where AGE $_{\mathrm{ij}}$ is a continuous covariate, $\operatorname{SEX}_{\mathrm{i}}$ is a 2-level factor and $\operatorname{DISEASE}_{\mathrm{ik}}(\mathrm{k}=1,2,3)$ are dummy variables representing the 4-level factor for underlying disease. Note that the the survival distribution is a truncated Weibull for censored observations as discussed in the mice example. The regression coefficients and the precision of the random effects $\tau$ are given independent "non-informative" priors, namely

$$
\begin{aligned}
& \mathrm{b}_{\mathrm{k}} \sim \operatorname{Normal}(0,0.0001) \\
& \tau \sim \operatorname{Gamma}(0.0001,0.0001)
\end{aligned}
$$

The shape parameter of the survival distribution $r$ is given a Gamma(1, 0.0001) prior which is slowly decreasing on the positive real line.

The graphical model and BUGS language are given below.

Graphical model for kidney example:


## BUGS language for kidney example

model
\{
for (i in $1: N$ ) \{
for (jin 1 : M) \{
\# Survival times bounded below by censoring times:
t[i,j] ~ dweib(r, mu[i,j]) I(t.cen[i, j], );
$\log (m u[i, j])<-$ alpha + beta.age * age[i, j]

+ beta.sex *sex[i]
+ beta.dis[disease[i]] + b[i];
\}
\# Random effects:
b[i] ~ dnorm(0.0, tau)
\}
\# Priors:
alpha $\sim \operatorname{dnorm}(0.0,0.0001)$;

```
    beta.age ~ dnorm(0.0, 0.0001);
    beta.sex ~ dnorm(0.0, 0.0001);
# beta.dis[1] <- 0; # corner-point constraint
    for(k in 2:4) {
        beta.dis[k] ~ dnorm(0.0, 0.0001);
    }
    tau ~ dgamma(1.0E-3, 1.0E-3);
    r ~ dgamma(1.0, 1.0E-3);
    sigma <- 1 / sqrt(tau); # s.d. of random effects
}
```


## Data (click to open )

Inits ( click to open )

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error val2.5pc |  | median | val97.5pc start | sample |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| alpha | -4.529 | 0.9036 | 0.06244 | -6.348 | -4.473 | -2.932 | 1001 | 10000 |
| beta.dis[2] | 0.1265 | 0.5679 | 0.01859 | -0.9922 | 0.1201 | 1.3 | 1001 | 10000 |
| beta.dis[3] | 0.5995 | 0.5781 | 0.02205 | -0.5284 | 0.5863 | 1.815 | 1001 | 10000 |
| beta.dis[4] | -1.198 | 0.8483 | 0.03147 | -2.805 | -1.206 | 0.5525 | 1001 | 10000 |
| beta.sex | -1.945 | 0.5019 | 0.028 | -3.054 | -1.906 | -1.042 | 1001 | 10000 |
| r | 1.205 | 0.1711 | 0.01523 | 0.9005 | 1.2 | 1.541 | 1001 | 10000 |
| sigma | 0.6367 | 0.3802 | 0.03159 | 0.04092 | 0.6494 | 1.366 | 1001 | 10000 |

## Leuk: Cox regression

Several authors have discussed Bayesian inference for censored survival data where the integrated baseline hazard function is to be estimated non-parametrically Kalbfleisch (1978) ,Kalbfleisch and Prentice (1980), Clayton (1991), Clayton (1994).Clayton (1994) formulates the Cox model using the counting process notation introduced by Andersen and Gill (1982) and discusses estimation of the baseline hazard and regression parameters using MCMC methods. Although his approach may appear somewhat contrived, it forms the basis for extensions to random effect (frailty) models, time-dependent covariates, smoothed hazards, multiple events and so on. We show below how to implement this formulation of the Cox model in BUGS.

For subjects $i=1, \ldots, n$, we observe processes $\mathrm{N}_{\mathrm{i}}(\mathrm{t})$ which count the number of failures which have occurred up to time $t$. The corresponding intensity process $l_{i}(t)$ is given by

$$
\mathrm{l}_{\mathrm{i}}(\mathrm{t}) \mathrm{dt}=\mathrm{E}\left(\mathrm{dN} \mathrm{~N}_{\mathrm{i}}(\mathrm{t}) \mid \mathrm{F}_{\mathrm{t}}-\right)
$$

where $d N_{i}(t)$ is the increment of $N_{i}$ over the small time interval $[t, t+d t)$, and $F_{t}$ - represents the available data just before time t . If subject $i$ is observed to fail during this time interval, $\mathrm{dN}_{\mathrm{i}}(\mathrm{t})$ will take the value 1 ; otherwise $\mathrm{dN}_{\mathrm{i}}(\mathrm{t})=0$. Hence $\mathrm{E}\left(\mathrm{dN}_{\mathrm{i}}(\mathrm{t}) \mid \mathrm{F}_{\mathrm{t}}\right)$ corresponds to the probability of subject $i$ failing in the interval $[t, t+d t)$. As $d t->0$ (assuming time to be continuous) then this probability becomes the instantaneous hazard at time $t$ for subject $i$. This is assumed to have the proportional hazards form

$$
I_{i}(t)=Y_{i}(t) \lambda_{0}(t) \exp \left(\beta \mathbf{z}_{i}\right)
$$

where $Y_{i}(t)$ is an observed process taking the value 1 or 0 according to whether or not subject $i$ is observed at time $t$ and $\lambda_{0}(t) \exp \left(\beta \mathbf{z}_{\mathbf{i}}\right)$ is the familiar Cox regression model. Thus we have observed data $D=N_{i}(t), Y_{i}(t), \mathbf{z}_{i} ; i=1, \ldots n$ and unknown parameters $\beta$ and $\Lambda_{0}(t)=\operatorname{Integral}\left(\lambda_{0}(u), u\right.$, $\mathrm{t}, 0$ ), the latter to be estimated non-parametrically.

The joint posterior distribution for the above model is defined by

$$
P\left(\boldsymbol{\beta}, \Lambda_{0}() \mid D\right) \sim P\left(D \mid \boldsymbol{\beta}, \Lambda_{0}()\right) P(\boldsymbol{\beta}) P\left(\Lambda_{0}()\right)
$$

For $B U G S$, we need to specify the form of the likelihood $P\left(D \mid \beta, \Lambda_{0}()\right)$ and prior distributions for $\boldsymbol{\beta}$ and $\Lambda_{0}()$. Under non-informative censoring, the likelihood of the data is proportional to

$$
\begin{aligned}
& \Pi\left[\Pi \mathrm{I}_{\mathrm{i}}(\mathrm{t})^{\mathrm{dN}} \mathrm{~N}_{\mathrm{i}}(\mathrm{t})\right] \exp \left(-\mathrm{I}_{\mathrm{i}}(\mathrm{t}) \mathrm{dt}\right) \\
& \mathrm{i}=1 \mathrm{t}>=0
\end{aligned}
$$

This is essentially as if the counting process increments $\mathrm{dN}_{\mathrm{i}}(\mathrm{t})$ in the time interval $[\mathrm{t}, \mathrm{t}+\mathrm{dt})$ are independent Poisson random variables with means $\mathrm{l}_{\mathrm{i}}(\mathrm{t}) \mathrm{dt}$ :

$$
d N_{i}(t) \sim \operatorname{Poisson}\left(l_{i}(t) d t\right)
$$

We may write

$$
l_{i}(t) d t=Y_{i}(t) \exp \left(\beta \mathbf{z}_{i}\right) d \Lambda_{0}(t)
$$

where $\mathrm{d} \Lambda_{0}(\mathrm{t})=\Lambda_{0}(\mathrm{t}) \mathrm{dt}$ is the increment or jump in the integrated baseline hazard function occurring during the time interval $[\mathrm{t}, \mathrm{t}+\mathrm{dt})$. Since the conjugate prior for the Poisson mean is the gamma distribution, it would be convenient if $\Lambda_{0}()$ were a process in which the increments $\mathrm{d} \Lambda_{0}(\mathrm{t})$ are distributed according to gamma distributions. We assume the conjugate independent increments prior suggested by Kalbfleisch (1978), namely

$$
\mathrm{d} \Lambda_{0}(\mathrm{t}) \sim \operatorname{Gamma}\left(\mathrm{cd} \Lambda_{0}{ }_{0}(\mathrm{t}), \mathrm{c}\right)
$$

Here, $\mathrm{d} \Lambda^{*}{ }_{0}(\mathrm{t})$ can be thought of as a prior guess at the unknown hazard function, with c representing the degree of confidence in this guess. Small values of c correspond to weak prior beliefs. In the example below, we set $\mathrm{d} \Lambda^{*}{ }_{0}(\mathrm{t})=\mathrm{rdt}$ where r is a guess at the failure rate per unit time, and dt is the size of the time interval.

The above formulation is appropriate when genuine prior information exists concerning the underlying hazard function. Alternatively, if we wish to reproduce a Cox analysis but with, say, additional hierarchical structure, we may use the multinomial-Poisson trick described in the $B U G S$ manual. This is equivalent to assuming independent increments in the cumulative 'noninformative' priors. This formulation is also shown below.

The fixed effect regression coefficients $\beta$ are assigned a vague prior

$$
\beta \sim \operatorname{Normal}(0.0,0.000001)
$$

BUGS language for the Leuk example:

```
model
{
# Set up data
    for(i in 1:N) {
        for(j in 1:T) {
```

```
    # risk set = 1 if obs.t >= t
            Y[i,j] <- step(obs.t[i] - t[j] + eps)
    # counting process jump = 1 if obs.t in [ t[j], t[j+1] )
    # i.e. if t[j] <= obs.t < t[j+1]
            dN[i, j] <- Y[i, j] * step(t[j + 1] - obs.t[i] - eps) * fail[i]
        }
    }
# Model
    for(j in 1:T) {
                for(i in 1:N) {
                    dN[i, j] ~ dpois(Idt[i, j]) # Likelihood
                    Idt[i, j] <- Y[i, j] * exp(beta * Z[i]) * dLO[j] # Intensity
        }
        dLO[j] ~ dgamma(mu[j], c)
        mu[j] <- dL0.star[j] * c # prior mean hazard
    # Survivor function = exp(-Integral{IO(u)du})^exp(beta*z)
        S.treat[j] <- pow(exp(-sum(dL0[1 : j])), exp(beta *-0.5));
        S.placebo[j] <- pow(exp(-sum(dL0[1 : j])), exp(beta * 0.5));
    }
    c <- 0.001
    r<- 0.1
    for (j in 1:T) {
            dLO.star[j] <- r * (t[j + 1] - t[j])
    }
    beta ~ dnorm(0.0,0.000001)
}
```

Data ( click to open)
Inits ( click to open )

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc | start | sample |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| S.placebo[1] | 0.9282 | 0.04863 | 5.004E-4 | 0.8094 | 0.9387 | 0.9907 | 1001 | 10000 |
| S.placebo[2] | 0.8538 | 0.06843 | 7.467E-4 | 0.6926 | 0.8639 | 0.9571 | 1001 | 10000 |
| S.placebo[3] | 0.8161 | 0.07561 | 7.661E-4 | 0.6422 | 0.8244 | 0.9362 | 1001 | 10000 |
| S.placebo[4] | 0.7432 | 0.08534 | 8.86E-4 | 0.5586 | 0.7503 | 0.8892 | 1001 | 10000 |
| S.placebo[5] | 0.6703 | 0.09256 | 9.762E-4 | 0.4749 | 0.6755 | 0.835 | 1001 | 10000 |
| S.placebo[6] | 0.5633 | 0.09747 | 9.302E-4 | 0.3666 | 0.5661 | 0.7477 | 1001 | 10000 |
| S.placebo[7] | 0.5304 | 0.09778 | 9.097E-4 | 0.338 | 0.5336 | 0.7148 | 1001 | 10000 |
| S.placebo[8] | 0.4142 | 0.09387 | 8.073E-4 | 0.2374 | 0.4119 | 0.6037 | 1001 | 10000 |
| S.placebo[9] | 0.3812 | 0.09325 | 8.172E-4 | 0.2086 | 0.3779 | 0.5701 | 1001 | 10000 |
| S.placebo[10] | 0.32 | 0.08945 | 8.307E-4 | 0.1583 | 0.315 | 0.509 | 1001 | 10000 |
| S.placebo[11] | 0.2583 | 0.0845 | 7.771E-4 | 0.111 | 0.2511 | 0.4395 | 1001 | 10000 |
| S.placebo[12] | 0.2257 | 0.08105 | 7.359E-4 | 0.08703 | 0.2181 | 0.402 | 1001 | 10000 |
| S.placebo[13] | 0.1956 | 0.07723 | 7.293E-4 | 0.06867 | 0.1873 | 0.3668 | 1001 | 10000 |
| S.placebo[14] | 0.1656 | 0.07326 | 6.788E-4 | 0.04889 | 0.1567 | 0.3298 | 1001 | 10000 |
| S.placebo[15] | 0.1398 | 0.06788 | 6.183E-4 | 0.03602 | 0.1305 | 0.2953 | 1001 | 10000 |
| S.placebo[16] | 0.0867 | 0.05455 | 5.259E-4 | 0.01301 | 0.07663 | 0.22 | 1001 | 10000 |
| S.placebo[17] | 0.04445 | 0.03913 | 4.092E-4 | 0.002506 | 0.03349 | 0.1484 | 1001 | 10000 |
| S.treat[1] | 0.983 | 0.01372 | 1.541E-4 | 0.9473 | 0.9866 | 0.9982 | 1001 | 10000 |
| S.treat[2] | 0.9643 | 0.02175 | $2.58 \mathrm{E}-4$ | 0.9115 | 0.9692 | 0.9922 | 1001 | 10000 |
| S.treat[3] | 0.9544 | 0.02538 | 3.003E-4 | 0.8918 | 0.9598 | 0.9884 | 1001 | 10000 |
| S.treat[4] | 0.9343 | 0.03217 | $4.071 \mathrm{E}-4$ | 0.8573 | 0.9398 | 0.9797 | 1001 | 10000 |
| S.treat[5] | 0.9125 | 0.03913 | 5.007E-4 | 0.821 | 0.9185 | 0.9701 | 1001 | 10000 |
| S.treat[6] | 0.8772 | 0.04896 | 6.526E-4 | 0.7654 | 0.8838 | 0.9521 | 1001 | 10000 |
| S.treat[7] | 0.8652 | 0.05234 | $6.984 \mathrm{E}-4$ | 0.745 | 0.8717 | 0.947 | 1001 | 10000 |
| S.treat[8] | 0.8178 | 0.06456 | 8.45E-4 | 0.6736 | 0.8246 | 0.9229 | 1001 | 10000 |
| S.treat[9] | 0.8024 | 0.06872 | 9.057E-4 | 0.6528 | 0.8099 | 0.9151 | 1001 | 10000 |
| S.treat[10] | 0.771 | 0.07613 | 9.916E-4 | 0.6064 | 0.7786 | 0.8976 | 1001 | 10000 |
| S.treat[11] | 0.7339 | 0.08462 | 0.001154 | 0.5522 | 0.7409 | 0.8774 | 1001 | 10000 |
| S.treat[12] | 0.7114 | 0.08897 | 0.001204 | 0.5224 | 0.7174 | 0.8659 | 1001 | 10000 |
| S.treat[13] | 0.6882 | 0.0932 | 0.001268 | 0.4913 | 0.6937 | 0.8528 | 1001 | 10000 |
| S.treat[14] | 0.6619 | 0.097 | 0.001318 | 0.4641 | 0.6669 | 0.8355 | 1001 | 10000 |
| S.treat[15] | 0.636 | 0.1007 | 0.00137 | 0.4318 | 0.6406 | 0.8191 | 1001 | 10000 |
| S.treat[16] | 0.5662 | 0.111 | 0.001493 | 0.3453 | 0.5688 | 0.773 | 1001 | 10000 |
| S.treat[17] | 0.4761 | 0.1189 | 0.001548 | 0.2502 | 0.4747 | 0.7085 | 1001 | 10000 |
| beta | 1.538 | 0.4176 | 0.005644 | 0.7718 | 1.521 | 2.384 | 1001 | 10000 |

## LeukFr: Cox regression with random effects

Freireich et al (1963)'s data presented in the Leuk example actually arise via a paired design. Patients were matched according to their remission status (partial or complete). One patient from each pair received the drug 6-MP whilst the other received the placebo. We may introduce an additional vector (called pair) in the BUGS data file to indicate each of the 21 pairs of patients.

We model the potential 'clustering' of failure times within pairs of patients by introducing a groupspecific random effect or frailty term into the proportional hazards model. Using the counting process notation introduced in the Leuk example, this gives

$$
\begin{aligned}
& \mathrm{l}_{\mathrm{i}}(\mathrm{t}) \mathrm{dt}=Y_{\mathrm{i}}(\mathrm{t}) \exp \left(\beta^{\prime} z_{i}+\mathrm{b}_{\text {pairi }_{i}}\right) \mathrm{d} \Lambda_{0}(\mathrm{t}) \quad \mathrm{i}=1, \ldots, 42 ; \quad \text { pair }_{\mathrm{i}}=1, \ldots, 21 \\
& \text { bpair } \sim \operatorname{Normal}(0, \tau)
\end{aligned}
$$

A non-informative Gamma prior is assumed for $\tau$, the precision of the frailty parameters. Note that the above 'additive' formualtion of the frailty model is equivalent to assuming multiplicative frailties with a log-Normal population distibution. Clayton (1991) discusses the Cox proportional hazards model with multiplicative frailties, but assumes a Gamma population distribution.

The modified BUGS code needed to include a fraility term in the Leuk example is shown below

```
model
\{
\# Set up data
    for(i in \(1: N)\{\)
        for(j in 1:T) \{
\# risk set = 1 if obs.t >= t
                Y[i, j] <- step(obs.t[i] -t[j] + eps)
\# counting process jump \(=1\) if obs.t in [t[j], t[j+1])
\# i.e. if \(t[j]<=\) obs.t \(<t[j+1]\)
            \(d N[i, j]<-Y[i, j]\) *step(t[j+1] - obs.t[i] - eps)*fail[i]
        \}
    \}
\# Model
    for(j in 1:T) \{
        for(i in \(1: N)\{\)
            dN[i, j] ~ dpois(ldt[i, j])
            Idt[i, j] <- Y[i, j] * exp(beta * Z[i]+b[pair[i]]) * dLO[j]
        \}
        dLO[j] ~ dgamma(mu[j], c)
```

```
            mu[j] <- dL0.star[j] * c # prior mean hazard
# Survivor function = exp(-Integra\{l0(u)du})^\operatorname{exp(beta *z)}
    S.treat[j] <- pow(exp(-sum(dL0[1 : j])), exp(beta * -0.5))
    S.placebo[j] <- pow(exp(-sum(dL0[1 : j])), exp(beta * 0.5))
    }
    for(k in 1: Npairs) {
    b[k] ~ dnorm(0.0, tau);
    }
    tau ~ dgamma(0.001, 0.001)
    sigma <- sqrt(1 / tau)
    c<-0.001 r<-0.1
    for (j in 1:T) {
        dL0.star[j] <- r * (t[j+1]-t[j])
    }
    beta ~ dnorm(0.0,0.000001)
}
```


## Data ( click to open)

Inits ( click to open)

## Results

A 1000 update burn in followed by a further 10000 updates gave the parameter estimates

|  | mean | sd | MC_error | val2.5pc | median | val97.5pc start | sample |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| beta | -1.607 | 0.4399 | 0.009042 | -2.507 | -1.592 | -0.7798 | 1001 |
| sigma | 0.2415 | 0.2255 | 0.01543 | 0.02854 | 0.1625 | 0.8548 | 1001 |

