

Eg Data Example using PKBugs and WinBUGS

Developing the model and running WinBUGS from PKBugs

Data files are supplied to allow users to start using WinBUGS from three points.

If you wish to start from scratch, i.e. from a NONMEM-type data file then start at '1'.

If you wish to start with the pre-made eg_labels.odc and eg_data.odc then start at '6'

If you wish to start with the pre-made PKBugs output then start at '17'.

The following steps are performed from the PKBugs tool box on the main WinBUGS menu.

- 1) Open the eg_data.dat file with an ascii text editor
- 2) Open a new window in WinBUGS (FILE then NEW)
- 3) Copy and paste the first row (the column headings) from eg_data.dat to the new window. Be sure to delete the '#' symbol, and save this (FILE then SAVE AS) eg_labels.odc.
- 4) Open another new window in WinBUGS (FILE then NEW)
- 5) Copy and paste the data from eg_data.dat into the new window and save this (FILE then SAVE AS) eg_data.odc.

- 6) Open the files eg_labels.odc (do this by selecting FILE then OPEN
- 7) Load item names (these are the column names for the data file). Do this by selecting Load item names from the pull down menu under PKBugs.
- 8) Close eg_labels.odc.
- 9) Open eg_data.odc (FILE OPEN). Load data. Do this by selecting Load data from the PKBugs menu item
- 10) Close eg_data.odc
- 11) Define model. Do this by selecting PKBugs Define model... select the PK model (1-compartment) and residual variance model (normal) and then confirm the structural and residual model by clicking Check Model. Close this menu box.
- 12) Priors. Select Priors from the pull down menu under PKBugs. Enter the prior estimates for each PK parameter (CL=6, 30%; V=18, 30%) as the population mean and between subject variability (assumed by PKBugs to be log normal). To do this click on the parameter and then enter the population mean and inter-individual cv (%). Clicking between parameters will toggle the different prior values. The window on the right of this dialogue box allows you to establish basic covariate relationships with parameters – since there are no covariates in this example this can be ignored. Click Done when complete and close grayed Define Priors box. PKBugs will generate the priors for you.
- 13) Load priors. Close Priors window. Initial values for population parameters will now be generated by PKBugs.
- 14) Load inits (pop). Close window. Initial values for theta (individual values of parameters) will now be generated by PKBugs.
- 15) Load inits (theta). Close window.

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PKBugs has now generated the model and data and is almost ready to run. We will run the model within WinBUGS (rather than using PKBugs) This allows you to edit any or all of the inputs you have made and to save the model and data to run at a later date.

Running the model within WinBUGS (Main menu items. No further need for PKBugs).

- 16) Use the **Print model** option and then save the model (e.g. eg_model_PKB.odc).¹
- 17) Double click on the word **model** in the open window and then select **Model** then **Specification** which will open a dialogue box. In this window select **check model**.²
- 18) Going back to the WinBUGS code double click on the first **list** statement and then select **load data** in the Specification Tool window.
- 19) Select **Compile**.
- 20) Using the scroll bar on the side of the WinBUGS code window scroll down about two thirds down the file to find the second **list** statement (refers "theta=structure"). Double click on **list**. Then **load inits** in the dialogue box.
- 21) Sometimes the **gen inits** will become grayed out at this stage. If not click **gen inits** (this means that some nodes in the model have not been provided with initial values). Then close the Specification Tool box. You may close the WinBUGS code now (assuming you have saved it).
- 22) From the main toolbox select **Inference** then **samples**. In the Sample Monitor Tool box enter each of the names of the parameters that you wish to monitor during the MCMC procedure into the node field and click on **set**. (in this example **mu**, **omega**, **sigma**, and **theta.mean** would be useful to select).
- 23) From the main pull down menu now select **Model** then **Update**. The updates option will be highlighted with '1000' – change this to a suitable number of iterations (e.g. 14 000 – recall that the first 4000 will be discarded as 'burn in').
- 24) Click "update" to start the MCMC procedure.
- 25) When the MCMC procedure has been completed the **update** box can be closed. Highlight the **Sample Monitor Tool** box (selected previously in point 7), select the parameter of interest and the relevant statistics can be viewed, including **stats**, **density**, **history**, **autoC** (autocorrelation) etc. Correlations between parameters may be assessed by selecting **Inference** then **Correlations** then in the **correlation tool** box enter a parameter (e.g. **mu**) in the first of the **node** boxes, when you do this you will be able to select **scatter** to look at the correlations between the parameters of that name (e.g. **mu[1]** vs. **mu[2]**). If you wish to look at the correlations between different parameter types then type one into the first **node** box (e.g. **mu**) and the other

¹ In the pre-made files the PKBugs print model is either available as 1 large file eg_model_data_inits.odc or as 3 separate files (eg_model.odc, eg_prior_data.odc and eg_inits.odc).

² The following instructions are based on using the single print model file (eg_model_data_inits.odc). If you use the 3 separate files then it is unnecessary to scroll down and it is also unnecessary to highlight 'model' or 'list' it is only required that at each stage you activate the window that contains the appropriate information.

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into the other node box (e.g. ω) – then select **scatter**. In this last option all correlations between all μ and ω parameters will be displayed.

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Priors

Population average CL = 6 L/h

Population average Vd = 18 L

Between-subject variability CL = 30%

Between-subject variability Vd = 30%

Residual variance = normal

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WinBUGS output

Model

```
model {
  for (i in 1:n.ind) {
    for (j in off.data[i]:(off.data[i + 1] - 1)) {
      data[j] ~ dnorm(model[j], tau)
      model[j] <- pk.model(1, theta[i, 1:p], time[j],
hist[off.hist[i]:(off.hist[i + 1] - 1), 1:n.col], pos[j])
    }
    theta[i, 1:p] ~ dnorm(theta.mean[i, 1:p], omega.inv[1:p, 1:p])
    theta.mean[i, 1] <- mu[1]
    theta.mean[i, 2] <- mu[2]
  }
  tau ~ dgamma(tau.a, tau.b)
  sigma <- 1 / sqrt(tau)
  mu[1:q] ~ dnorm(mu.prior.mean[1:q], mu.prior.precision[1:q, 1:q])
  omega.inv[1:p, 1:p] ~ dwish(omega.inv.matrix[1:p, 1:p], omega.inv.dof)
  for (i in 1:p) {
    for (j in 1:p) {
      omega[i, j] <- inverse(omega.inv[1:p, 1:p], i, j)
    }
  }
}
```

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Output

Statistics:

node	mean	sd	MC error	2.5%	median	97.5%	start	sample
mu[1]	1.772	0.054	7.975E-4	1.666	1.772	1.879	4001	16000
mu[2]	2.882	0.06561	8.891E-4	2.752	2.882	3.012	4001	16000

node	mean	sd	MC error	2.5%	median	97.5%	start	sample
omega[1,1]	0.08281	0.0242	2.498E-4	0.04738	0.07894	0.1413	4001	16000
omega[1,2]	0.07111	0.02508	2.144E-4	0.03348	0.06723	0.1321	4001	16000
omega[2,1]	0.07111	0.02508	2.144E-4	0.03348	0.06723	0.1321	4001	16000
omega[2,2]	0.1279	0.03638	3.094E-4	0.07465	0.1222	0.2146	4001	16000

node	mean	sd	MC error	2.5%	median	97.5%	start	sample
sigma	0.686	0.04466	7.978E-4	0.6054	0.6839	0.78	4001	16000

Density



