Random effects in AD Model Builder

ADMB-RE user guide

admb-project.org

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License

Contents

Preface

A few comments about notation: Important points are emphasized with a star

★ like this.

Please submit all comments and complaints by email to users@admb-project.org.

Chapter 1

Introduction

This document is a user's guide to random effects modelling in AD Model Builder (ADMB). Random effects is feature of ADMB, in the same way as profile likelihoods are, but sufficiently complex to merit a separate user manual. The work on the random effects "module" (ADMB-RE) started around 2003. The pre-existing part of ADMB (and its evolution) is referred to as "ordinary" ADMB in the following. This manual refers to version 9.0.x of ADMB and (ADMB-RE).

Before you start with random effects it is recommended that you have some experience with ordinary ADMB. This manual tries to be self contained, but it is clearly an advantage if you have written (and successfully run) a few tpl-files. Ordinary ADMB is described in the ADMB manual (ADMB Development Core Team 2009) which is available from admb-project.org. If you are new to ADMB, but have experience with C++ (or a similar programming language) you may benefit from taking a look at the quick references in Appendix D.

ADMB-RE is very flexible. The term "random effect" seems to indicate that it only can handle mixed-effect regression type models, but this is very misleading. "Latent variable" module would have been a more precise term. It can be argued ADMB-RE is the most flexible latent variable framework around. All the mixed model stuff in software packages such that R, Stata, SPSS, etc. allow only very specific models to be fit, and it is impossible to change the distribution of the random effects, say, if you wanted to do that. The NLMIXED macro in SAS is more flexible, but cannot handle state-space models or models with crossed random effects. WinBUGS is the only exception, which with it ability to handle discrete latent variables, is a bit more flexible than ADMB-RE. However, WinBUGS does all its computations using MCMC exclusively, while ADMB-RE lets the user choose between maximum likelihood estimation (which in general is much faster) and MCMC.

An important part of the ADMB-RE documentation is the example collection which is described in Appendix A. As with the example collections for ADMB and AUTODIF, you will find fully worked examples including data and code for the model. The examples have been selected to illustrate the various aspects of ADMB-RE, and are frequently referred to troughout this manual.

1.1 Summary of features

Why use AD Model Builder for creating nonlinear random effects models? The answer consists of three words – flexibility, speed and accuracy. To illustrate these points a number of examples comparing ADMB-RE with two existing packages NLME which runs on R and Splus, and WinBUGS. In general NLME is rather fast and it is good for the problems for which it was designed, but it is quite inflexible. What is needed is a tool with at least the computational power of NLME but the flexibility to deal with arbitrary nonlinear random effects models. In section 2.4 we consider a thread from the R user list where a discussion about extending a model to use random effects which had a log-normal rather than normal distribution took place. This appeared to be quite difficult. With ADMB-RE this change takes one line of code. WinBUGS on the other hand is very flexible and many random effects models can be easily formulated in it. However, it can be very slow and it is necessary to adopt a Bayesian perspective which may be a problem for some applications. A model which runs 25 times faster under ADMB than under WinBUGS may be found in A.1.1.

Model formulation With ADMB you can formulate and fit a large class of nonlinear statistical models. With ADMB-RE you can include random effects in your model. Examples of such models include:

- Generalized linear mixed models (logistic and Poisson regression).
- Nonlinear mixed models (growth curve models, pharmacokinetics).
- State space models (nonlinear Kalman filters).
- Frailty models in survival analysis.
- Nonparametric smoothing.
- Semiparametric modelling.

- Frailty models in survival analysis.
- Bayesian hierarchical models.
- General nonlinear random effects models (fisheries catch-at-age models).

You formulate the likelihood function in a template file, using a language that resembles C++. The file is compiled into an executable program (Linux or Windows). The whole C++ language is to your disposal, giving you great flexibility with respect to model formulation.

Computational basis of ADMB-RE

- Hyper-parameters (variance components etc.) estimated by maximum likelihood.
- Marginal likelihood evaluated by the Laplace approximation or importance sampling.
- Exact derivatives calculated using Automatic Differentiation.
- Sampling from the Bayesian posterior using MCMC (Metropolis-Hastings algorithm).
- Most features of ordinary ADMB (matrix arithmetic and standard errors, etc.) are available.
- Sparse matrix libraries useful for Markov random fields and crossed random effects are available.

The strengths of ADMB-RE

- *Flexibility*: You can fit a large variety of models within a single framework.
- *Convenience*: Computational details are transparent. Your only responsibility is to formulate the loglikelihood
- *Computational efficiency*: ADMB-RE is up to 50 times faster than WinBUGS.
- *Robustness*: With exact derivatives you can fit highly nonlinear models.
- *Convergence diagnostic*: The gradient of the likelihood function provides a clear convergence diagnostic.

Program interface

- *Model formulation*: You fill in a C++ based template using your favorite text editor.
- *Compilation*: You turn your model into an executable program using a C++ compiler (which you need to install separately).
- *Platforms*: Windows and Linux

How to obtain ADMB-RE ADMB-RE is a module for ADMB. Both can be obtained from admb-project.org

Chapter 2

The language and the program

2.1 What is ordinary ADMB?

ADMB is a software package for doing parameter estimation in nonlinear models. It combines a flexible mathematical modelling language (built on C++) with a powerful function minimizer (based on Automatic Differentiation). The following features of ADMB make it very useful for building and fitting nonlinear models to data:

- Vector-matrix arithmetic, vectorized operations for common mathematical functions.
- Read and write vector and matrix objects to file.
- Fit the model is a stepwise manner (with 'phases'), where more and more parameters become active in the minimization.
- Calculate standard deviations of arbitrary functions of the model parameters by the 'delta method'.
- MCMC sampling around the posterior mode.

To use random effects in ADMB it is recommended that you have some experience in writing ordinary ADMB programs. In this sections we review, for the benefit of the reader without this experience, the basic constructs of ADMB.

Model fitting with ADMB has three stages: 1) Model formulation, 2) Compilation and 3) Program execution. The model fitting process is typically iterative: After having looked at the output from stage 3) one goes back to stage 1) and modifies some aspect of the program.

Writing an ADMB program To fit a statistical model to data we must carry out certain fundamental tasks, such as reading data from file, declaring the set of parameters that should be estimated, and finally we must give a mathematical description of the model. In ADMB you do all of this by filling in a template, which is an ordinary text file with the file-name extension '.tpl' (and hence the template file is known as the tpl-file). You therefore need a text editor, such as 'vi' under Linux or 'Notepad' under Windows, to write the tpl-file. The first tpl-file to which the reader of the ordinary ADMB manual is exposed is `simple.tpl` (listed in Section 2.3 below). We shall use `simple.tpl` as our generic tpl-file, and we shall see that introduction of random effects only requires small changes to the program.

A tpl-file is divided into a number of 'sections', each representing one of the fundamental tasks mentioned above. The required sections are:

Name	**Purpose**
`DATA_SECTION`	Declare 'global' data objects; initialization from file
`PARAMETER_SECTION`	Declare independent parameters
`PROCEDURE_SECTION`	Specify model and objective function in C++

More details are given when we later look at `simple.tpl`, and a quick reference card is available in Appendix D.

Compiling an ADMB program After having finished writing `simple.tpl`, we want to convert it into an executable program. This is done in a DOS-window under Windows, and in an ordinary terminal window under Linux. To compile `simple.tpl`, we would under both platforms give the command:

```
$ admb -r simple
```

Here, '`$`' is the command line prompt (which may be a different symbol on your computer), and `-r` is an option telling the program `admb` that your model contains random effects. The program `admb` accepts another option `-s` which produces the 'safe' (but slower) version of the executable program. The `-s` option should be used in a debugging phase, but it should be skipped when the final production version of the program is generated.

The compilation process really consists of two steps: first `simple.tpl` is converted to a C++ program by a preprosessor called `tpl2rem` in the case of ADMB-RE and `tpl2cpp` in the case of ordinary ADMB (Appendix D). An error message from `tpl2rem` consists of a single line of text, with a reference to the line in the tpl-file where the error occurs. If successful, the first compilation step results in the C++ file `simple.cpp`. In the second step `simple.cpp` is compiled and linked using an ordinary C++ compiler (which is not part of

ADMB). Error messages during this phase typically consist of long printouts, with references to line numbers in `simple.cpp`. To track down syntax errors it may occasionally be useful to look at the content of `simple.cpp`. When you understand what is wrong in `simple.cpp` you should go back and correct `simple.tpl` and re-enter the command `admb -r simple`. When all errors have been removed, the result will be an executable file, which is called `simple.exe` under Windows or `simple` under Linux. The compilation process is illustrated in Figure D.1.

Running an ADMB-program The executable program is run in the same window as it was compiled. Note that data are not usually part of the ADMB program (`simple.tpl`). Instead, data are being read from a file with the file name extension '.dat' (`simple.dat`). This brings us to the naming convention used by ADMB programs for input and output files: The executable automatically infers file names by adding an extension to its own name. The most important files are:

	File name	**Contents**
Input	`simple.dat`	Data for the analysis
	`simple.pin`	Initial parameter values
Output	`simple.par`	Parameter estimates
	`simple.std`	Standard deviations
	`simple.cor`	Parameter correlations

You can use command line options to modify the behavior of the program at runtime. The available command line options can be listed by typing:

```
$ simple -?
```

(or whatever your executable is called). The command line options that are specific to ADMB-RE are listed in Appendix C, and are discussed in detail under the various sections. An option you probably will like to use during an experimentation phase is `-est`, which turns off calculation of standard deviations, and hence reduces the running time of the program.

ADMB-IDE: Easy and efficient user interface The graphical user interphase to ADMB by Arni Magnusson simplifies the process of building and running the model, especially for the beginner (ADMB Foundation 2009). Among other things, it provides syntax highlighting and links error messages from the C++ compiler to the `.cpp` file.

Initial values The initial values can be provided in different ways (see the ordinary ADMB manual). Here we only describe the `.pin` file approach. The `.pin` file should contain legal values (within the bounds) for all the parameters, including the random effects. The values must be given in the same order as the parameters are defined in the `.tpl` file . The easiest way of generating a `.pin` file with the right structure is to first run the program with an `-maxfn 0` option (for this you do not need a `.pin` file) and copy the resulting `.p01` file into `.pin` file, and edit it to provide the correct numeric values. More information about what initial values for random effects really means is given in Section 3.7.

2.2 Why random effects?

Many people are familiar with the method of least squares for parameter estimation. Far fewer know about random effects modeling. The use of random effects requires that we adopt a statistical point of view, where the sum of squares is interpreted as being part of a likelihood function. When data are correlated, the method of least squares is sub-optimal, or even biased. But relax, random effects come to rescue!

The classical motivation of random effects is:

- To create parsimonious and interpretable correlation structures.
- To account for additional variation or overdispersion.

We shall see, however, that random effects are useful in a much wider context. For instance, in non-parametric smoothing (**??**).

Statistical prerequisites To use random effects in ADMB you must be familiar with the notion of a random variable, and in particular with the normal distribution. In case you are not, please consult a standard textbook in statistics. The notation $u \sim N(\mu, \sigma^2)$ is used throughout this manual, and means that u has a normal (Gaussian) distribution with expectation μ and variance σ^2. The distribution placed on the random effects is called the 'prior', which is a term borrowed from Bayesian statistics.

A central concept that originates from generalized linear models is that of a linear predictor. Let $x_1, \ldots, x_p$ denote observed covariates (explanatory variables), and let $\beta_1, \ldots, \beta_p$ be the corresponding regression parameters to be estimated. Many of the examples in this manual involve a linear predictor $\eta_i = \beta_1 x_{1,i} + \cdots + \beta_p x_{p,i}$, which we also will write on vector form as $\eta = \mathbf{X}\beta$.

Frequentist or Bayesian statistics? A pragmatic definition of a frequentist is a person who prefers to estimate parameters by the method of maximum likelihood. Similarly, a Bayesian is a person who use MCMC techniques to generate samples from the posterior distribution (typically with noninformative priors on hyper-parameters), and from these samples generates some summary statistic such as the posterior mean. With its `-mcmc` runtime option ADMB lets you switch freely between the two worlds. The approaches complement each other rather than being competitors. A maximum likelihood fit (point estimate + covariance matrix) is a step-1 analysis. For some purposes step-1 is sufficient. In other situations, one may want to see posterior distributions for the parameters. In such situations the established covariance matrix (inverse Hessian of the log-likelihood) is used by ADMB to implement an efficient Metropolis-Hastings algorithm (which you invoke with `-mcmc`).

A simple example We use the `simple.tpl` example from the ordinary ADMB manual to exemplify the use of random effects. The statistical model underlying this example is the simple linear regression

$$Y_i = ax_i + b + \varepsilon_i, \qquad i = 1, \ldots, n,$$

where Y_i and x_i are the data, a and b are the unknown parameters to be estimated, and $\varepsilon_i \sim N(0, \sigma^2)$ is an error term.

Consider now the situation that we do not observe x_i directly, but rather we observe

$$X_i = x_i + e_i,$$

where e_i is a measurement error term. This situation frequently occurs in observational studies, and is known as the 'error in variables' problem. Assume further that $e_i \sim N(0, \sigma_e^2)$, where σ_e^2 is the measurement error variance. For reasons discussed below, we shall assume that we know the value of σ_e, so we shall pretend that $\sigma_e = 0.5$.

Because x_i is not observed, we model it as a random effect with $x_i \sim N(\mu, \sigma_x^2)$. In ADMB-RE you are allowed to make such definitions through the new parameter type `random_effects_vector`. (There is also a `random_effects_matrix` which allows you to define a matrix of random effects).

1. Why do we call x_i a random effect, while we do not use this term for X_i and Y_i (though they clearly are 'random')? The point is that X_i and Y_i are observed directly, while x_i is not. The term 'random effect' comes from regression analysis, where it means a random regression coefficient. In a more general context 'latent random variable' is probably a better term.

2. The unknown parameters in our model are: a, b, μ, σ, σ_x and $x_1, \ldots, x_n$. We have agreed to call $x_1, \ldots, x_n$ random effects. The rest of the parameters are called hyper-parameters. Note that we place no prior distribution on the hyper-parameters.

3. Random effects are integrated out of the likelihood, while hyper-parameters are estimated by maximum likelihood . This approach is often called 'empirical Bayes', and will be considered a frequentist method by most people. There is however nothing preventing you from making it 'more Bayesian' by putting priors (penalties) on the hyper-parameters.

4. A statistician will say "this model is nothing but a bivariate Gaussian distribution for (X, Y), and we don't need any random effects in this situation". This is formally true, because we could work out the covariance matrix of (X, Y) by hand and fit the model using ordinary ADMB. This program would probably run much faster, but it would have taken us longer to write the code without declaring x_i to be of type `random_effects_vector`. But, more important is that random effects can be used also in non-Gaussian (nonlinear) models where we are unable to derive an analytical expression for the distribution of (X, Y).

5. Why didn't we try to estimate σ_e? Well, let us count the parameters in the model: a, b, μ, σ, σ_x and σ_e; totally six parameters. We know that the bivariate Gaussian distribution has only five parameters (the means of X and Y and three free parameters in the covariate matrix). Thus, our model is not identifiable if we also try to estimate σ_e. Instead, we pretend that we have estimated σ_e from some external data source. This example illustrates a general point in random effects modelling: you must be careful to make sure that the model is identifiable!

2.3 A code example

Here is the random effects version of `simple.tpl`:

```
DATA_SECTION
 init_int nobs
 init_vector Y(1,nobs)
 init_vector X(1,nobs)

PARAMETER_SECTION
```

```
 init_number a
 init_number b
 init_number mu
 vector pred_Y(1,nobs)
 init_bounded_number sigma_Y(0.000001,10)
 init_bounded_number sigma_x(0.000001,10)
 random_effects_vector x(1,nobs)
 objective_function_value f

PROCEDURE_SECTION            // This section is pure C++
 f = 0;
 pred_Y=a*x+b;               // Vectorized operations

 // Prior part for random effects x
 f += -nobs*log(sigma_x) - 0.5*norm2((x-mu)/sigma_x);

 // Likelihood part
 f += -nobs*log(sigma_Y) - 0.5*norm2((pred_Y-Y)/sigma_Y);
 f += -0.5*norm2((X-x)/0.5);

 f *= -1; // ADMB does minimization!
```

Comments

1. Everything following '//' is a comment.
2. In the `DATA_SECTION`, variables with a `init_` in front of the data type are read from file.
3. In the `PARAMETER_SECTION`
   - Variables with a `init_` in front of the data type are the hyper-parameters, i.e. the parameters to be estimated by maximum likelihood.
   - `random_effects_vector` defines the random effect vector (there is also a `random_effects_matrix`). There can be more than one such object, but they must all be defined after the hyper-parameters, otherwise you will get an error message from the preprocessor `tpl2rem`.
   - Objects that neither are hyper-parameters or random effects are ordinary programming variables that can be used in the `PROCEDURE_SECTION`. For instance, we can assign a value to the vector `pred_Y`.

- The objective function should be defined as the last variable.

4. The `PROCEDURE_SECTION` basically consists of standard C++ code which primary purpose is to calculate the value of the objective function.
   - Variables defined in `DATA_SECTION` and `PARAMETER_SECTION` may be used.
   - Standard C++ functions as well as special ADMB functions, such as `norm2(x)` (which calculates $\sum x_i^2$), may be used.
   - Often the operations are vectorized, as in the case of `simple.tpl`
   - The objective function should be defined as the last variable.
   - ADMB does minimization, rather than optimization. Thus, the sign of the loglikelihood function `f` is changed in the last line of the code.

Parameter estimation We learned above that hyper-parameters are estimated but maximum likelihood, but what if we also are interested in the value of the random effects? For this purpose ADMB-RE offers an 'empirical Bayes' approach, which involves fixing the hyper-parameters at their maximum likelihood estimates, and treating the random effects as the parameters of the model. ADMB-RE automatically calculates 'maximum posterior' estimates of the random effects for you. Estimates of both hyper-parameters and random effects are written to `simple.par`.

2.4 The flexibility of ADMB-RE

Say that you doubt the distributional assumption $x_i \sim N(\mu, \sigma_x^2)$ that was made in `simple.tpl`, and that you want to check if a skewed distribution gives a better fit. You could for instance take

$$x_i = \mu + \sigma_x \exp(z_i), \qquad z_i \sim N(0,1).$$

Under this model the standard deviation of x_i is proportional to, but not directly equal to σ_x. It is easy to make this modification in `simple.tpl`. In the `PARAMETER_SECTION` we replace the declaration of `x` by

```
vector x(1,nobs)
random_effects_vector z(1,nobs)
```

and in the PROCEDURE_SECTION we replace the prior on x by

```
f = - 0.5*norm2(z);
x = mu + sigma_x*exp(z);
```

This example shows one of the strengths of ADMB-RE: it is very easy to modify models. In principle you can implement any random effects model you can think of, but as we shall discuss later, there are limits to the number of random effects you can declare.

Chapter 3

Random effects modeling

This chapter describes all ADMB-RE features, except those related to "separability" which are dealt with in Chapter 4. Separability, or the Markov property as it is called in statistics, is a property possessed by many model classes allows ADMB-RE to generate more efficient executable programs. However, most ADMB-RE concepts and techniques are better learned and understood without introducing separability. Throughout much of this chapter we will refer to the program `simple.tpl` from Section 2.3.

3.1 The objective function

As with ordinary ADMB the user specifies an objective function in terms of data and parameters, but in ADMB-RE the objective function must have the interpretation of being a (negative) log-likelihood. One typically has got a hierarchical specification of the model, where at the top layer data are assumed to have a certain probability distribution conditionally on the random effects (and the hyper-parameters), and at the next level the random effects are assigned a prior distribution (typically normal). Because conditional probabilities are multiplied to yield the joint distribution of data and random effects, the objective function becomes a sum of (negative) log-likelihood contributions, and the following rule applies

★ The order in which the different loglikelihood contributions are added to the objective function does not matter.

An addition to this rule is that all programming variables have got their value assigned before they enter in a prior or a likelihood expression. WinBUGS users must take care when porting their programs to ADMB because this is not required in WinBUGS.

The reason why the **negative** log-likelihood is used is that ADMB for historical reasons does minimization (as opposed to maximization). In complex models, with contributions to the log-likelihood coming from a variety of data sources and random effects priors, it is recommended that you collect the contributions to the objective function using the `-=` operator of C++, i.e.

```
f -= -nobs*log(sigma_x) - 0.5*norm2((x-mu)/sigma_x);
```

By using `-=` instead of `+=` you do not have to change the sign of every likelihood expression, which would be a likely source of error. When non of the advanced features of Chapter 4 are used, you are allowed to switch the sign of the objective function at the end of the program

```
f *= -1; // ADMB does minimization!
```

so that in fact `f` can hold the value of the log-likelihood until the last line of the program.

It is OK to ignore constant terms ($0.5\log(2\pi)$ for the normal distribution) as we did in `simple.tpl`. This only affects the objective function value, not any other quantity reported in the `.par` and `.std` (not even the gradient value).

3.2 The random effects distribution (prior)

In `simple.tpl` we declared $x_1, \ldots, x_n$ to be of type `random_effects_vector`. This statement tells ADMB that $x_1, \ldots, x_n$ should be treated as random effects (i.e. be the targets for the Laplace approximation), but it does not say anything about which distribution the random effects should have. We assumed that $x_i \sim N(\mu, \sigma_x^2)$, and (without saying it explicitly) that the x_i's were statistically independent. We know that the corresponding prior contribution to the loglikelihood is

$$-n\log(\sigma_x) - \frac{1}{2\sigma_x^2}\sum_{i=1}(x_i-\mu)^2\,.$$

with ADMB implementation

```
f += -nobs*log(sigma_x) - 0.5*norm2((x-mu)/sigma_x);
```

Both the assumption about independence and normality can be generalized, as we shortly will do, but first we introduce a transformation technique that forms the basis for much of which follows later.

Scaling of random effects A frequent source of error when writing ADMB-RE programs is that priors get wrongly specified. The following trick can make the code easier to read, and has the additional advantage of being numerically stable for small values of σ_x. From basic probability theory we know that if $u \sim N(0,1)$, then $x = \sigma_x u + \mu$ will have a $N(\mu, \sigma_x^2)$ distribution. The corresponding ADMB code would be

```
f += - 0.5*norm2(u);
x = sigma_x*u + mu;
```

(This, of course, requires that we change the type of `x` from `random_effects_vector` to `vector`, and that `u` is declared as a `random_effects_vector`.)

The trick here was to start with a $N(0,1)$ distributed random effect `u` and to generate random effects `x` with another distribution. This is a special case of a transformation. Had we used a non-linear transformation we would have got a `x` with a non-gaussian distribution. The way we obtain correlated random effects is also transformation based. However, as we shall see in Chapter 4 transformation may "break" the separability of the model, so there are limitations to what transformations can do for you.

3.3 Correlated random effects

In some situation you will need correlated random effects, and as part of your problem you may want to estimate the elements of the covariance matrix. A typical example is mixed regression where the intercept random effect (u_i) is correlated with the slope random effect (v_i),

$$y_{ij} = (a + u_i) + (b + v_i)\, x_{ij} + \varepsilon_{ij}.$$

(If you are not familiar with the notation, please consult an introductory book on mixed regression, such Pinheiro & Bates (2000).) In this case we can define correlation matrix

$$C = \begin{bmatrix} 1 & \rho \\ \rho & 1 \end{bmatrix},$$

and we want to estimate ρ along with the variances of u_i and v_i. Here it is trivial to ensure that C is positive definite, by requiring $-1 < \rho < 1$, but in higher dimensions this issue requires more careful consideration.

To ensure that C is positive definite you can parameterize the problem in terms of the Cholesky factor L, i.e. $C = LL'$, where L is a lower diagonal matrix with positive diagonal elements. There are $q(q-1)/2$ free parameters (the non-zero elements of L) to be estimated, where q is the dimension of C.

Since C is a correlation matrix we must ensure that its diagonal elements are unity. An example with $q = 4$ is

```
PARAMETER_SECTION
  matrix L(1,4,1,4)                 // Cholesky factor
  init_vector a(1,6)                // Free parameters in C
  init_bounded_vector B(1,4,0,10)   // Standard deviations

PROCEDURE_SECTION

  int k=0;
  L(1,1) = 1.0;
  for(i=2;i<=4;i++)
  {
    L(i,i) = 1.0;
    for(j=1;j<=i-1;j++)
      L(i,j) = a(k++);
    L(i)(1,i) /= norm(L(i)(1,i));  // Ensures that C(i,i) = 1
  }
```

Given the Cholesky factor L, we can proceed in different directions. One option is to use the same transformation-of-variable technique as above: Start out with a vector u of independent $N(0, 1)$ distributed random effects. Then, the vector

```
  x = L*u;
```

has correlation matrix $C = LL'$. Finally, we multiply each component of `x` by the appropriate standard deviation:

```
  y = elem_prod(x,sigma);
```

Large structured covariance matrices In some situations, for instance in spatial models, q will be large ($q = 100$, say). Then it is better to use the approach outlined in Section 4.5.

3.4 Non-Gaussian random effects

Usually, the random effects will have a Gaussian distribution, but technically speaking there is nothing preventing you from replacing the normality assumption, such as

```
f -= -nobs*log(sigma_x) - 0.5*norm2((x-mu)/sigma_x);
```

with a log gamma density, say. It can however be expected that the Laplace approximation will be less accurate when you move away from normal priors. Hence, you should instead use the transformation trick that we learned earlier, but now with a non-linear transformation. A simple example of this yielding a log-normal prior was given in Section 2.4.

Say you want x to have cumulative distribution function $F(x)$. It is well known that you achieve this by taking $x = F^{-1}(\Phi(u))$, where Φ is the where Φ is the cumulative distribution function of the $N(0,1)$ distribution. For a few common distributions, the composite transformation $F^{-1}(\Phi(u))$ has been coded up for you in ADMB-RE, and all you have to do is:

1. Define a random effect u with a $N(0,1)$ distribution.
2. Transform u into a new random effect x using one of `something_deviate` functions described below.

where `something` is the name of the distribution.

As an example, say we want to obtain av vector `x` of gamma distributed random effects (probability density $x^{a-1}\exp(-x)/\Gamma(a)$). We can then use the code:

```
PARAMETER_SECTION
  init_number a                                 // Shape parameter
  init_number lambda                            // Scale parameter
  vector x(1,n)
  random_effects_vector u(1,n)
  objective_function_value g

PROCEDURE_SECTION
  g -= -0.5*norm2(u);                           // N(0,1) likelihood contr.
  for (i=1;i<=n;i++)
    x(i) = lambda*gamma_deviate(u(i),a);
```

Full example: http://www.otter-rsch.com/admbre/examples/gamma/gamma.html

Similarly, to obtain beta(a,b) distributed random effects, with density $f(x) \propto x^{a-1}(1-x)^{b-1}$, we use:

```
PARAMETER_SECTION
```

```
  init_number a
  init_number b

PROCEDURE_SECTION
  g -= -0.5*norm2(u);                          // N(0,1) likelihood contr.
  for (i=1;i<=n;i++)
    x(i) = beta_deviate(u(i),a,b);
```

The function `beta_deviate()` has a fourth (optional) parameter that controls the accuracy of the calculations. To learn more about this you will have to dig into the source code. You find the code for `beta_deviate()` in the file `df1b2betdev.cpp`. The mechanism for specifying default parameter values are found in the source file `df1b2fun.h`.

A third example is provided by the "robust" normal distribution with probability density

$$f(x) = 0.95\frac{1}{\sqrt{2\pi}}e^{-0.5x^2} + 0.05\frac{1}{c\sqrt{2\pi}}e^{-0.5(x/c)^2}$$

where c is a "robustness" parameter which by default is set to $c = 3$ in `df1b2fun.h`. Note that this is a mixture distribution consisting of 95% $N(0,1)$ and 5% $N(0,c^2)$. The corresponding ADMB-RE code is

```
PARAMETER_SECTION
  init_number sigma                          // Standard deviations (almost)
  number c

PROCEDURE_SECTION
  g -= - 0.5*norm2(u);  // N(0,1) likelihood contribution from u's
  for (i=1;i<=n;i++)
  {
    x(i) = sigma*robust_normal_mixture_deviate(u(i),c);
  }
```

Can a, and c be estimate? As indicated by the data types used above:

- ★ a and b are among the parameters that are being estimated.
- ★ c cannot be estimated.

It would however be possible to write a version of `robust_normal_mixture_deviate` where also c and the mixing proportion (fixed at 0.95 here) can be estimated. For this you need to look into the file `df1b2norlogmix.cpp`. The list of distribution that can be used is likely to be expanded in the future.

Density	Expression	Parameters	Name
Poisson	$\frac{\mu^x}{\Gamma(x+1)}e^{-\mu}$	$\mu > 0$	`log_density_poisson`
Neg. binomial[1]	$\mu = E(X)$, $\tau = \frac{Var(X)}{E(X)}$	$\mu, \tau > 0$	`log_negbinomial_density`

Table 3.1: Distributions which currently can be used as high-level data distributions (for data X) in ADMB-RE. [1]The expression for the negative binomial distribution is omitted due to its somewhat complicated form. Instead the parameterization, via the via the overdispersion coefficient, is given. The interested reader can look at the actual implementation in the source file `df1b2negb.cpp`

3.5 Built in data likelihoods

In simple `simple.tpl` the mathematical expressions for all log-likehood contributions where written out in full detail. You may have hoped that for the most common probability distributions there were functions written so that you do not have to remember or look up their log-likelihood expressions. In case your density are among those given in Table 3.1 you are lucky. More functions are likely to be implemented over time, and user contributions are welcomed!

We stress that these functions should be only be used for data likelihoods, and in fact, they will not compile if you try to let X be a random effect. So for instance, if you have observations x_i that are Poisson distributed with expectation μ_i you would write

```
for (i=1;i<=n;i++)
  f -= og\_density\_poisson(x(i),mu(i));
```

Note that functions do not accept vector arguments.

3.6 Phases

A very useful feature of ADMB is that it allows the model to be fit in different phases. In the first phase you estimate only a subset of the parameters, with the remaining parameters being fixed at their initial values. In the second phase more parameters are turned on, and so it goes. The phase in which a parameter becomes active is specified in the declaration of the parameter. By default a parameter has phase 1. A simple example would be

```
PARAMETER_SECTION
```

```
init_number a(1)
random_effects_vector b(1,10,2)
```

where `a` becomes active in phase 1, while `b` is a vector of length 10 that becomes active in phase 2. With random effects we have the following rule-of-thumb (which may not always apply):

Ph1 Activate all parameters in the data likelihood, except those related to random effects.

Ph2 Activate random effects and theirs standard deviations.

Ph3 Activate correlation parameters (of random effects)

In complicated models it may be useful to break Ph1 into several sub-phases.

During program development it is often useful to be able to completely switch a parameters off. A parameter is inactivated when given phase '-1' as in

```
PARAMETER_SECTION
  init_number c(-1)
```

The parameter is still part of the program, and its value will still be read from the pin-file, but it does not take part in the optimization (in any phase).

For further details about phases, please consult the section 'Carrying out the minimization in a number of phases' in the ADMB manual (ADMB Development Core Team 2009).

3.7 Penalized likelihood and empirical Bayes

The main question we answer in this section is: how are the random effects estimated, i.e. how are the values that enters the `.par` and `.std` calculated? Along the way we will learn a little about how ADMB-RE works internally.

By now you should be familiar with the statistical interpretation of the random effects, but how are they treated internally in ADMB-RE? Since the random effects are not observed data they have parameter status, but we distinguish them from the hyper-parameters. In the marginal likelihood function used internally by ADMB-RE to estimate hyper-parameters, the random effects are 'integrated out'. The purpose of the integration is to generate the marginal probability distribution for the observed quantities, which are X and Y in `simple.tpl`. In that example we could have found an analytical expression for the marginal distribution of (X, Y), because only normal distributions

were involved. For other distributions, such as the binomial, no simple expression for the marginal distribution exists, and hence we must rely on ADMB to do the integration. In fact, the core of what ADMB-RE does for you is to automatically calculates the marginal likelihood, in its effort to estimate the hyper-parameters.

The integration technique used by ADMB-RE is the so-called Laplace approximation (Skaug & Fournier 2006). Somewhat simplified, the algorithm involves iterating between the following two steps:

1. The 'penalized likelihood' step: Maximizing the likelihood with respect to the random effects, while holding the value of the hyper-parameters fixed. In `simple.tpl` this means doing the maximization w.r.t. `x` only.

2. Updating the value of the hyper-parameters, using the estimates of the random effects obtained in 1).

The reason for calling the objective function in 1) a penalized likelihood, is that the prior on the random effects acts as a penalty function.

We can now return to the role of the initial values specified for the random effects in the `.pin` file. Each time step 1) above is performed these values are used, unless you use the command line option `-noinit`, in which case the previous optimum is used as the starting value.

Empirical Bayes is commonly used to refer to Bayesian estimates of the random effects, with the hyper-parameters fixed at their maximum likelihood estimates. ADMB-RE uses maximum aposteriori Bayesian estimates, as evaluated in step 1) above. Posterior expectation is a more commonly used as Bayesian estimator, but it requires additional calculations, and is currently not implemented in ADMB-RE. For more details, see Skaug & Fournier (2006).

The classical criticism of empirical Bayes is that the uncertain about the hyper-parameters is ignored, and hence that the total uncertainty about the random effects is underestimated. ADMB-RE does however take this into account and uses the following formula

$$\mathrm{cov}(u) = -\left[\frac{\partial^2 \log p(u|\mathrm{data};\theta)}{\partial u \partial u'}\right]^{-1} + \frac{\partial u}{\partial \theta}\mathrm{cov}(\theta)\left(\frac{\partial u}{\partial \theta}\right)', \qquad (3.1)$$

where u is the vector of random effect, θ is the vector of hyper-parameters, and $\partial u/\partial\theta$ is the sensitivity of the penelized likelihood estimator on the value of θ. The first term on the r.h.s. is the ordinary Fisher information based variance of u, while the second term accounts for the uncertainty in θ.

3.8 Building a random effects model that works

In all nonlinear parameter estimation problems, there are two possible explanations when your program does not produce meaningful results:

1. The underlying mathematical model is not well defined, e.g. it may be over-parameterized.

2. You have implemented the model incorrectly, e.g. you have forgotten a minus sign somewhere.

In an early phase of the code development it may not be clear which of these is causing the problem. With random effects, the two-step iteration scheme described above makes it even more difficult to find the error. We therefore advise you always to check the program on simulated data before you apply it to your real dataset. This section gives you a recipe for how to do this.

The first thing you should do after having finished the tpl-file is to check that the penalized likelihood step is working correctly. In ADMB it is very easy to switch from a random effects version of the program to a penalized likelihood version. In `simple.tpl` we would simply redefine the random effects vector `x` to be of type `init_vector`. The parameters would then be a, b, μ, σ, σ_x and $x_1, \ldots, x_n$. It is not recommended, or even possible, to estimate all of these simultaneously, so you should fix σ_x (by giving it a phase '-1') at some reasonable value. The actual value at which you fix σ_x is not critically important, and you could even try a range of σ_x values. In larger models there will be more than one parameter that needs to be fixed. We recommend the following scheme:

1. Write a simulation program (in R, S-Plus, Matlab, or some other program) that generates data from the random effects model (using some reasonable values for the parameters) and writes to `simple.dat`.

2. Fit the penalized likelihood program with σ_x (or the equivalent parameters) fixed at the value used to simulate data.

3. Compare the estimated parameters with the parameter values used to simulate data. In particular, you should plot the estimated $x_1, \ldots, x_n$ against the simulated random effects. The plotted points should center around a straight line. If they do (to some degree of approximation) you most likely have got a correct formulation of the penalized likelihood.

If your program passes this test, you are ready to test the random effects version of the program. You redefine `x` to be of type `random_effects_vector`, free up σ_x, and apply again your program to the same simulated dataset. If the program produces meaningful estimates of the hyper-parameters, you most likely have implemented your model correctly, and you are ready to move on to your real data!

With random effects it often happens that the maximum likelihood estimate of a variance component is zero ($\sigma_x = 0$). Parameters bouncing against the boundaries usually makes one feel uncomfortable, but with random effects the interpretation of $\sigma_x = 0$ is clear and unproblematic. All it really means is that data do not support a random effect, and the natural consequence is to remove (or inactivate) $x_1, \ldots, x_n$, together with the corresponding prior (and hence σ_x), from the model.

3.9 MCMC

There are two different MCMC methods built into ADMB-RE: `-mcmc` and `-mcmc2`. Both are based on the Metropolis-Hastings algorithm. The former generates a Markov chain on the hyper-parameters only, while `-mcmc2` generates a chain on the joint vector of hyper-parameters and random effects. (Some sort of rejection sampling could be used with `-mcmc` to generate values also for the random effects, but this is currently not implemented). The advantages of `-mcmc` are:

- Because there typically is a small number of hyper-parameters, but a large number of random effects, it is much easier to judge convergence of the chain generated by `-mcmc` than that generated by `-mcmc2`.
- The `-mcmc` chain mixes faster than the `-mcmc2` chain.

The disadvantage of the `-mcmc` option is that it is slow, because it relies on evaluation of the marginal likelihood by the Laplace approximation. It is recommended to run (separately) both of `-mcmc` and `-mcmc2` to verify that they yield the same posterior for the hyper-parameters.

3.10 Importance sampling

The Laplace approximation may be inaccurate in some situations . The accuracy may be improved by adding an importance sampling step. This is done in ADMB-RE by using the command line argument `-is N seed`, where `N` is

the sample size in the importance sampling and `seed` (optional) is used to initialize the random number generator. Increasing `N` will give better accuracy, at the cost of a longer run time. As a rule-of-thumb you should start with `N=100`, and increase `N` stepwise by a factor of 2 until the parameter estimates stabilize.

By running the model with different seeds you can check the Monte Carlo error in your estimates, and possibly average across the different runs to decrease the Monte Carlo error. Replaing the `-is N seed` option with a `-isb N seed` gives you a "balanced" sample, which in general should reduce the Monte Carlo error.

For large values of `N`, the option `-is N seed` will require a lot of memory, and you will see that huge temporary files are produced during the execution of the program. The option `-isf 5` will split the calculations relating to importance sampling into 5 (or any number you like) batches. In combination with the techniques discussed in Section 3.12.1, this should reduce the storage requirements. An example of a command line is:

```
lessafre -isb 1000 9811 -isf 20 -cbs 50000000 -gdb 50000000
```

The `-is` option can also be used as a diagnostic tool for checking the accuracy of the Laplace approximation. If you add the `-isdiag` (print importance sampling) the importance sampling weights will be printed at the end of the optimization process. If these weights do not vary much, the Laplace approximation is probably doing well. On the other hand, if a single weight dominates the others by several orders of magnitude, you are in trouble, and it is likely that even `-is N` with a large value of `N` is not going to help you out. In such situations, reformulating the model, with the aim of making the loglikelihood closer to a quadratic function in the random effects, is the way to go. See also the following section.

3.11 REML (Restricted maximum likelihood)

It is well known that maximum likelihood estimators of variance parameters can be downwards biased. The biases arises from estimation of one or more mean-related parameters. The simplest example of a REML estimator is the ordinary sample variance

$$s^2 = \frac{1}{n-1}\sum_{i=1}^{n}(x_i - \bar{x})^2,$$

where the divisor $(n-1)$, rather the n which occurs for the maximum likelihood estimator, accounts for the fact that we have estimated a single mean parameter.

There are many ways of deriving the REML correction, but in the current context the most natural explanation is that we integrate the likelihood function (note: not the log-likelihood) with respect to the mean parameters β, say. This is achieved in ADMB-RE by defining β as being of type `random_effects_vector`, but without specifying a distribution/prior for the parameters. It should be noted that the only thing that the `random_effects_vector` statement tells ADMB-RE is that the likelihood function should be integrated with respect to β. In linear-Gaussian models the Laplace approximation is exact, and hence this approach yields exact REML estimates. In nonlinear models the notion of REML is more difficult, but REML-like corrections are still being used. For linear-Gaussian models the REML likelihood is available in closed form. Also many linear models can be fitted with standard software packages. It is typically much simpler to formulate a hierarchical model with explicit latent variables. As mentioned, the Laplace approximation is exact for Gaussian models, so it does not matter what way you do it.

An example of such a model is found at http://otter-rsch.com/admbre/examples/bcb/bcb.html. To make the executable program run efficiently, the command line options `-nr 1 -sparse` should be used for linear models. Also, note that REML estimates can be obtained as explained in section 3.11.

3.12 Improving performance

In this section we discuss certain mechanisms you can use to make an ADMB-RE program run faster and more smoothly.

3.12.1 Reducing the size of temporary files

When ADMB needs more temporary storage than is available in the allocated memory buffers, it starts producing temporary files. Since writing to disk is much slower than accessing memory, it is important to reduce the size of temporary files as much as possible. There are several parameters (such as `arrmblsize`) built into ADMB that regulates how large memory buffers an ADMB program allocates at startup. With random effects the memory requirements increase dramatically, and ADMB-RE deals with this by producing (when needed) six temporary files:

File name	Command line option
f1b2list1	-l1 N
f1b2list12	-l2 N
f1b2list13	-l3 N
nf1b2list1	-nl1 N
nf1b2list12	-nl2 N
nf1b2list13	-nl3 N

The table also shows the command line arguments you can use to manually set the size (determined by N) of the different memory buffers.

When you see any of these files start growing, you should kill your application and restart it with the appropriate command line options. In addition to the options shown above there is `-ndb N` that splits the computations into N chunks. This effectively reduces the memory requirements by a factor of N, at the cost of a somewhat longer run time. It is necessary that N is a divisor of the total number of random effects in the model, so that it is possible to split the job into N equally large parts. The `-ndb` option can be used in combination with the `-l` and `-nl` options listed above. The following rule-of-thumb for setting N in `-ndb N` can be used: if there are totally m random effects in the model, one should choose N such that $m/N \approx 50$. For most of the models in the example collection (Chapter 3) this choice of N prevents any temporary files of being created.

Consider the model `http://otter-rsch.com/admbre/examples/union/union.html` as an example. This model contains only about 60 random effects, but does rather heavy computations with these, and as a consequence large temporary files are generated. The following command line

```
$ ./union -l1 10000000 -l2 100000000 -l3 10000000 -nl1 10000000
```

takes away the temporary files but requires 80Mb of memory. The command line

```
$ ./union -est -ndb 5 -l1 10000000
```

also runs without temporary files, requires only 20Mb of memory, but runs three times slower.

Finally, a warning about the use of these command line options. If you allocate too much memory your application will crash, and you will (should) get a meaningful error message. You should monitor the memory use of your application using "Task Manager" under Windows and the command "top" under Linux, to ensure that you do not exceed the available memory on your computer.

3.12.2 Limited memory Newton optimization

The penalized likelihood step (Section 3.7), that forms a crucial part of the algorithm used by ADMB to estimate hyper-parameters, is by default conducted using a quasi-Newton optimization algorithm. If the number of random effects is large, as it typically is for separable models, it may be more efficient to use a 'limited memory quasi-Newton' optimization algorithm. This is done using the command line argument `-ilmn N`, where `N` is the number of steps to keep. Typically `N=5` is a good choice.

Chapter 4

Exploiting separability

The following model classes:

- Grouped or nested random effects
- State-space models
- Crossed random effects
- Latent Markov random fields

share an important property: their "Hessian" is a sparse matrix. This enables ADMB-RE to do the calculations very efficiently. The Hessian H is defined as the (negative) Fisher information matrix (inverse covariance matrix) of the posterior distribution of the random effects:

$$p(u|y) \propto p(y|u)p(u), \tag{4.1}$$

where u are the random effect and y are the data. This definition is only excact if both u and y are Gaussian. More generally, H is the Hessian matrix of the function $\log[p(\cdot|y)]$.

That H is sparse means that it contains mostly zeros. The actual sparsity pattern depends on the model type:

- Grouped or nested random effects: H is block diagonal.
- State-space models: H is a banded matrix with a narrow band.
- Crossed random effects: unstructured sparsity pattern.
- Latent Markov random fields: often banded, but with a wide band.

ADMB-RE should print out a message such as

```
Block diagonal Hessian (Block size = 3)
```

at the beginning of the phase when the random effects are becoming active parameters.

Not all models are separable, and for small toy examples (less than 50 random effects, say) we do not need to care about separability. But chances are high that you need to become familiar with the concept. How do we inform ADMB-RE that the model is separable? We shall see the key is `SEPARABLE_FUNCTION`'s, which are invoked many times with a small number of the random effects as arguments each time. Do you think that ADMB-RE should be able to detect the separable structure on its own? Well, maybe so, but after you have worked with a few separable models you will find that having to call the `SEPARABLE_FUNCTION`'s actually structures your own way of thinking about the model. This is especially so for state-space models. A good reference (although a bit advanced) on conditional probabilities is Rue & Held (2005).

4.1 The first example

A simple example is the one-way variance component model

$$y_{ij} = \mu + \sigma_u u_i + \varepsilon_{ij}, \qquad i = 1, \ldots, q, \quad j = 1, \ldots, n_i$$

where $u_i \sim N(0, 1)$ is a random effect and $\varepsilon_{ij} \sim N(0, \sigma^2)$ is an error term. The straightforward implementation of this model (shown only in part) is

```
PARAMETER_SECTION
  random_effects_vector u(1,q)

PROCEDURE_SECTION
  for(i=1;i<=q;i++)
  {
    g -= -0.5*square(u(i));
    for(j=1;j<=n(i);j++)
      g -= -log(sigma) - 0.5*square((y(i,j)-mu-sigma_u*u(i))/sigma);
  }
```

The efficient implementation of this model is

```
PROCEDURE_SECTION
  for(i=1;i<=q;i++)
    g_cluster(i,u(i),mu,sigma,sigma_u);

SEPARABLE_FUNCTION void g_cluster(int i, const dvariable& u,...)
  g -= -0.5*square(u);
  for(int j=1;j<=n(i);j++)
    g -= -log(sigma) - 0.5*square((y(i,j)-mu-sigma_u*u)/sigma);
```

where ... replaces the rest of the argument list (due to lack of space in this document).

It is the function call `g_cluster(i,u(i),mu,sigma,sigma_u)` that enables ADMB-RE to identify that the posterior distribution (4.1) factors (over i):

$$p(u|y) \propto \prod_{i=1}^{q} \left\{ \prod_{j=1}^{n_i} p(u_i|y_{ij}) \right\}$$

and hence that the Hessian is block diagonal (with block size 1). Knowing that the Hessian is block diagonal enables ADMB-RE to do a series of univariate Laplace approximations, rather than a single Laplace approximation in full dimension q. It should then be possible to fit models where q is in the order of thousands, but this clearly depends on the complexity of the function `g_cluster`.

The following rules apply:

★ The argument list in the definition of the `SEPARABLE_FUNCTION` should not broken into several lines of text in the tpl-file. This is often tempting as the line typically gets long, but it results in an error message from `tpl2rem`.

★ Objects defined in the `PARAMETER_SECTION` must be passed as arguments to `g_cluster`. There is one exception: the objective function `g` is a global object, and does not need to be an argument. Temporary/programming variables should be defined locally within the `SEPARABLE_FUNCTION`.

★ Objects defined in the `DATA_SECTION` should not be passed as arguments to `g_cluster` (they are also global objects).

The data types that currently can be passed as arguments to a `SEPARABLE_FUNCTION` are:

```
int
const dvariable&
const dvar_vector&
const dvar_matrix&
```

with an example being

```
SEPARABLE_FUNCTION void f(int i, const dvariable& a, const dvar_vector& beta)
```

The qualifier `const` is required for the latter two data types, and signalizes to the C++ compiler that the value of the variable is not going to be changed by the function. You may also come across the type `const prevariable&` which means exactly the same as `const dvariable&`.

There are other rules that have to be obeyed:

★ No calculations involving variables defined in the `PARAMETER_SECTION` are allowed in the `PROCEDURE_SECTION`. The only use of such variables there is passing them as arguments to `SEPARABLE_FUNCTION`'s.

This rule implies that all the action has to take place inside the `SEPARABLE_FUNCTION`'s. To minimize the number of parameters that have be passed as arguments, the following programming practice is recommended when using `SEPARABLE_FUNCTION`'s:

★ The `PARAMETER_SECTION` should contain definitions only of the independent parameters (those variables which type has a `init_` prefix) and random effects, i.e. no temporary programming variables.

All temporary variables needed for the computations should be defined locally in the `SEPARABLE_FUNCTION` as shown here:

```
SEPARABLE_FUNCTION void prior(const dvariable& log_s, const dvariable& u)
  dvariable sigma_u = exp(log_s);
  g -= -log_s - 0.5*square(u(i)/sigma_u);
```

Full example http://otter-rsch.com/admbre/examples/orange/orange.html. The orange model has block size 1,

4.2 Nested or clustered random effects: Block diagonal H

In the above model there was no hierarchical structure among the latent random variables (the `u`'s). A more complicated example is provided by the

following model:

$$y_{ijk} = \sigma_v v_i + \sigma_u u_{ij} + \varepsilon_{ijk}, \qquad i = 1, \ldots, q, \quad j = 1, \ldots, m, \quad k = 1, \ldots, n_{ij},$$

where the random effects v_i and u_{ij} are independent $N(0,1)$ distributed, and $\varepsilon_{ijk} \sim N(0, \sigma^2)$ is still the error term. One often says that the `u`'s are nested within the `v`'s.

Another perspective is that the data can be split into independent clusters. For $i_1 \neq i_2$ we have that y_{i_1jk} and y_{i_2jk} are statistically independent, so that the likelihood factors at the outer nesting level (i).

To exploit this we use the `SEPARABLE_FUNCTION` as follows:

```
PARAMETER_SECTION
  random_effects_vector v(1,q)
  random_effects_matrix u(1,q,1,m)

PROCEDURE_SECTION
  for(i=1;i<=q;i++)
    g_cluster(v(i),u(i),sigma,sigma_u,sigma_v,i);
```

Note that `u(i)` is the i'th row of the matrix `u` (this is standard ADMB stuff), and it should be passed as a vector to the `SEPARABLE_FUNCTION`, which we would implement as follows:

```
SEPARABLE_FUNCTION void g_cluster(const dvariable& v,const dvar_vector& u,...)
  g -= -0.5*square(v);
  g -= -0.5*norm2(u);

  for(int j=1;j<=m;j++)
    for(int k=1;k<=n(i,j);k++)
      g -= -log(sigma) - 0.5*square((y(i,j,k)
                -sigma_v*v - sigma_u*u(j))/sigma);
```

★ For a model to be detected as "Block diagonal Hessian" each latent variable should be passed exactly once as an argument to a `SEPARABLE_FUNCTION`.

To ensure that you have not broken this rule you should look for an message like this at run time:

```
  Block diagonal Hessian (Block size = 3)
```

It is possible that the groups or clusters (as indexed by i in this case) are of different size. Then the "Block diagonal Hessian" that is printed is an average.

Alternative, we could have structured the program as follows:

```
PARAMETER_SECTION
  random_effects_vector v(1,q)
  random_effects_matrix u(1,q,1,m)

PROCEDURE_SECTION
  for(i=1;i<=q;i++)
    for(j=1;j<=m;j++)
      g_cluster(v(i),u(i,j),sigma,sigma_u,sigma_u,i);
```

but this would not be detected by ADMB-RE as a clustered model (because `v(i)` is passed multiple times), and hence ADMB-RE will not be able to take advantage of the fact that the likelihood factors. However, the use of the `SEPARABLE_FUNCTION` makes it possible for ADMB-RE to perform efficient calculations when invoked with the `-shess` command line option as described later.

4.2.1 Gauss-Hermite quadrature

In the situation where the model is separable of type "block diagonal Hessian" with only a single random effect in each block (see Section 4), Gauss-Hermite quadrature is available as an option to the Laplace approximation and the `-is` option (importance sampling). It is invoked with command line option `-gh N` where `N` is the number of quadrature points.

4.2.2 Frequency weighting for multinomial likelihoods

In situations were the response variable only can take on a finite number of different values, it is possibly to reduce the computational burden enormously. As an example, consider a situation where observation y_i is binomially distributed with parameters $N = 2$ and p_i. Assume that

$$p_i = \frac{\exp(\mu + u_i)}{1 + \exp(\mu + u_i)},$$

where μ is a parameter and $u_i \sim N(0, \sigma^2)$ is a random effect. For independent observations $y_1, \ldots, y_n$, the loglikelihood function for the parameter $\theta = (\mu, \sigma)$

can be written:

$$l(\theta) = \sum_{i=1}^{n} \log\left[p(x_i;\theta)\right]. \tag{4.2}$$

In ADMB-RE $p(x_i;\theta)$ is approximated using the Laplace approximation. However, since y_i only can take the values 0, 1 and 2, we can re-write the loglikelihood as

$$l(\theta) = \sum_{j=0}^{2} n_j \log\left[p(j;\theta)\right],$$

where n_j is the number y_i's being equal to j. Still the Laplace approximation must be used to approximate $p(j;\theta)$, but now only for $j = 0, 1, 2$, as opposed to n times above. For large n this can give large a large reduction in computing time.

To implement the weighted loglikelihood (A.5) we define a weight vector $(w_1, w_2, w_3) = (n_0, n_1, n_2)$. To read the weights from file, and to tell ADMB-RE that `w` is a weights vector, the following code is used:

```
DATA_SECTION
 init_vector w(1,3)

PARAMETER_SECTION
 !! set_multinomial_weights(w);
```

In addition it is necessary to explicitly multiply the likelihood contributions in (A.5) by w. The program must be written with `SEPARABLE_FUNCTION` as explained in Section 4.2. For the likelihood (A.5) the `SEPARABLE_FUNCTION` will be invoked three times.

Full example: http://www.otter-rsch.com/admbre/examples/weights/weights.html

4.3 State-space models: Banded H

A simple state space model is

$$\begin{aligned} y_i &= u_i + \epsilon_i, \\ u_i &= \rho u_{i-1} + e_i, \end{aligned}$$

where $e_i \sim N(0, \sigma^2)$ is an innovation term. The log-likelihood contribution coming from the state vector $(u_1, \ldots, u_n)$ is

$$\sum_{i=2}^{n} \log\left(\frac{1}{\sqrt{2\pi}\sigma}\exp\left[-\frac{(u_i - \rho u_{i-1})^2}{2\sigma^2}\right]\right),$$

where $(u_1, \ldots, u_n)$ is the state vector. To make ADMB-RE exploit this special structure we write a `SEPARABLE_FUNCTION` named `g_conditional`, that implements the individual terms in the above sum. This function would then be invoked as follows

```
for(i=2;i<=n;i++)
  g_conditional(u(i),u(i-1),rho,sigma);
```

Full example http://www.otter-rsch.com/admbre/examples/polio/polio.html.

Above we have looked at a model with a univariate state vector. For multivariate state vectors, as in

$$\begin{aligned} y_i &= u_i + v_i + \epsilon_i, \\ u_i &= \rho_1 u_{i-1} + e_i, \\ v_i &= \rho_2 v_{i-1} + d_i, \end{aligned}$$

we would merge the u and v vectors into a single vector $(u_1, v_1, u_2, v_2, \ldots, u_n, v_n)$, and define

```
random_effects_vector u(1,m)
```

where $m = 2n$. The call to the `SEPARABLE_FUNCTION` would now look like

```
for(i=2;i<=n;i++)
 g_conditional(u(2*(i-2)+1),u(2*(i-2)+2),u(2*(i-2)+3),u(2*(i-2)+4),...);
```

where `...` denotes the arguments ρ_1, ρ_2, σ_e and σ_d.

4.4 Crossed random effects: sparse H

The simplest instance of a crossed random effects model is

$$y_k = \sigma_u u_{i(k)} + \sigma_v v_{j(k)} + \varepsilon_k, \qquad i = 1, \ldots n,$$

where $u_1, \ldots, u_N$ and $v_1, \ldots, v_M$ are random effects, and where $i(k) \in \{1, N\}$ and $j(k) \in \{1, M\}$ are index maps. The y's sharing either a u or a v will be dependent, and in general no complete factoring of the likelihood will be possible. However, it is still important to exploit the fact that the u's and v's only enter the likelihood through pairs $(u_{i(k)}, v_{j(k)})$. Here is the code for the crossed model:

```
for (k=1;k<=n;k++)
 log_lik(k,u(i(k)),v(j(k)),mu,s,s_u,s_v);

SEPARABLE_FUNCTION void log_lik(int k, const dvariable& u,...)
 g -= -log(s) - 0.5*square((y(k)-(mu + s_u*u + s_v*v))/s);
```

If only a small proportion of all the possible combinations of u_i and v_j actually occurs in the data, then the posterior covariance matrix of $(u_1, \ldots, u_N, v_1, \ldots, v_M)$ will be sparse. When an executable program produced by ADMB-RE is invoked with the `-shess` command line option, sparse matrix calculations are used.

This is useful not only for crossed models. Here are a few other applications:

- For the nested random effects model as explained in section 4.2.
- REML estimation; recall that REML estimates are obtained by making a fixed effect random, but with no prior distribution. For the nested models in section 4.2, and the models with state-space structure of section 4.3, when using REML, ADMB-RE will to detect the cluster or time series structure of the likelihood. (This has to do with the implementation of ADMB-RE, not the model itself). However, the posterior covariance will still be sparse, and the use of `-shess` is advantageous.

4.5 Gaussian priors and quadratic penalties

In most models the prior for the random effect will be Gaussian. In some situations, such as in spatial statistics, all the individual components of the random effects vector will be jointly correlated. ADMB contains a special feature (the `normal_prior` keyword) for dealing efficiently with such models. The construct used to declaring a correlated Gaussian prior is

```
random_effects_vector u(1,n)
normal_prior S(u);
```

The first of these lines is an ordinary declaration of a random effects vector. The second line tells ADMB that `u` has a multivariate Gaussian distribution with zero expectation and covariance matrix `S` , i.e. the probability density of $\mathbf{u}$ is

$$h(\mathbf{u}) = (2\pi)^{-\dim(S)/2} \det(S)^{-1/2} \exp\left(-\frac{1}{2}\mathbf{u}' S^{-1} u\right).$$

Here, S is allowed to depend on the hyper-parameters of the model. The part of the code where `S` gets assigned its value must be placed in a `SEPARABLE_FUNCTION` (see

- ★ The log-prior $\log(h(\mathbf{u}))$ is automatically subtracted from the objective function. It is thus necessary that the objective function holds the negative loglikelihood when using the `normal_prior`.
- ★ To verify that your model really is partially separable you should try replacing the `SEPARABLE_FUNCTION` keyword with an ordinary `FUNCTION`. Then verify on a small subset of your data that the two versions of the program produce the same results. You should be able to observe that the `SEPARABLE_FUNCTION`-version runs faster.

Full example `http://otter-rsch.com/admbre/examples/spatial/spatial.html`).

Appendix A

Example collection

This section contains various examples of how to use ADMB-RE. Some of these has been referred to earlier in the manual. The exampels are grouped according to their "Hessian type" (see Section 4). At the end of each example you will find a **Files** section containing links to webpages where both program code and data can be downloaded.

A.1 Non-separable models

This section contains models which do not use any of the separability stuff. Sections A.1.2 and A.1.3 illustrate how to use splines as non-parametric compoents. This is currenlty a very popular technqiue, and fits very nicely into the random effects framework (Ruppert, Wand & Carroll 2003). All the models, except the first, are in fact separable, but for illustrative purposes (the code becomes easier to read) this has been ignored.

A.1.1 Mixed logistic regression; a WinBUGS comparison

Mixed regression regression models will usually have a block diagonal Hessian du to grouping/clustering of the data. The present model was deliberately chosen not to be separable, in order to pose a computational challenge to both ADMB-RE and WinBUGS.

Model description Let $\mathbf{y} = (y_1, \ldots, y_n)$ be a vector of dichotomous observations ($y_i \in \{0, 1\}$), and let $\mathbf{u} = (u_1, \ldots, u_q)$ be a vector of independent random effects, each with Gaussian distribution (expectation 0 and variance σ^2). Define the success probability $\pi_i = \Pr(y_i = 1)$. The following relationship between π_i and explanatory variables (contained in matrices $\mathbf{X}$ and $\mathbf{Z}$) is assumed:

$$\log\left(\frac{\pi_i}{1-\pi_i}\right) = \mathbf{X}_i\beta + \mathbf{Z}_i\mathbf{u},$$

where $\mathbf{X}_i$ and $\mathbf{Z}_i$ are the i'th rows of the known covariates matrices $\mathbf{X}$ $(n \times p)$ and $\mathbf{Z}$ $(n \times q)$, respectively, and β is a p-vector of regression parameters. Thus, the vector of fixed-effects vector is $\theta = (\beta, \log\sigma)$.

Results The goal here is to compare computation times with BUGS on a simulated data set. For this purpose we use $n = 200$, $p = 5$, $q = 30$, and values of the the hyper parameters as shown in the table below ('True values'). The matrices $\mathbf{X}$ and $\mathbf{Z}$ were generated randomly with each element uniformly distributed on $[-2, 2]$. As start values for both AD Model Builder and BUGS we used $\beta_{\text{init},j} = -1$ and $\sigma_{\text{init}} = 4.5$. In BUGS we used a uniform $[-10, 10]$ prior on β_j and a standard (in the BUGS literature) noninformative gamma prior on $\tau = \sigma^{-2}$. In AD Model Builder the parameter bounds $\beta_j \in [-10, 10]$ and $\log\sigma \in [-5, 3]$ were used in the optimization process.

	β_1	β_2	β_3	β_4	β_5	σ
True values	0.0000	0.0000	0.0000	0.0000	0.0000	0.1000
ADMB-RE	0.0300	-0.0700	0.0800	0.0800	-0.1100	0.1700
Std. dev.	0.1500	0.1500	0.1500	0.1400	0.1600	0.0500
WinBUGS	0.0390	-0.0787	0.0773	0.0840	-0.1041	0.1862

On the simulated dataset AD Model Builder used 27 seconds to converge to the optimum of likelihood surface. On the same dataset we first ran WinBUGS (Version 1.4) for 5,000 iterations. The recommended convergence diagnostic in WinBUGS is the Gelman-Rubin plot (see the help files available from the

menues in WinBUGS) which require that two Markov chains are run in parallel. From the Gelman-Rubin plot it was clear that convergence appeared after approximately $2,000$ iterations. The time taken by WinBUGS to perform generate the first $2,000$ was approximately 700 seconds.

Files http://otter-rsch.com/admbre/examples/logistic/logistic.html

A.1.2 Generalized additive models (GAM's)

Model description A very useful generalization of the ordinary multiple regression

$$y_i = \mu + \beta_1 x_{1,i} + \cdots + \beta_p x_{p,i} + \varepsilon_i,$$

is the class of additive models,

$$y_i = \mu + f_1(x_{1,i}) + \cdots + f_p(x_{p,i}) + \varepsilon_i. \tag{A.1}$$

Here, the f_j are 'nonparametric' components which can be modelled by penalized splines. When this generalization is carried over to generalized linear models, and we arrive at the class of GAM's (Hastie & Tibshirani 1990). From a computational perspective penalized splines are equivalent to random effects, and thus GAM's fall naturally into the domain of ADMB-RE.

For each component f_j in (A.1) we construct a design matrix $\mathbf{X}$ such that $f_j(x_{i,j}) = \mathbf{X}^{(i)}\mathbf{u}$, where $\mathbf{X}^{(i)}$ is the ith row of $\mathbf{X}$ and $\mathbf{u}$ is a coeffisient vector. We use the R-function `splineDesign` (from the `splines` library) to construct a design matrix $\mathbf{X}$. To avoid overfitting we add a first order difference penalty (Eilers & Marx 1996) :

$$-\lambda^2 \sum_{k=2} (u_k - u_{k-1})^2, \tag{A.2}$$

to the ordinary GLM loglikelihood, where λ is a smoothing parameter to be estimated. By viewing $\mathbf{u}$ as a random effects vector with the above Gaussian prior, and by taking λ as a hyper-parameter, it becomes clear that GAM's are naturally handled in ADMB-RE.

Implementation details

- A computationally more efficient implementation is obtained by moving λ from the penalty term to the design matrix, i.e. $f_j(x_{i,j}) = \lambda^{-1}\mathbf{X}^{(i)}\mathbf{u}$.
- Since (A.2) does not penalize the mean of $\mathbf{u}$, we impose the restriction that $\sum_{k=1} u_k = 0$ (see the `union.tpl` for details). Without this restriction the model would be over-parameterized since we allready have an overall mean μ in (A.1).
- To speed up computations the parameter μ (and other regression parameters) should be given 'phase 1' in ADMB, while the λ's and the $\mathbf{u}$'s should be given given 'phase 2'.

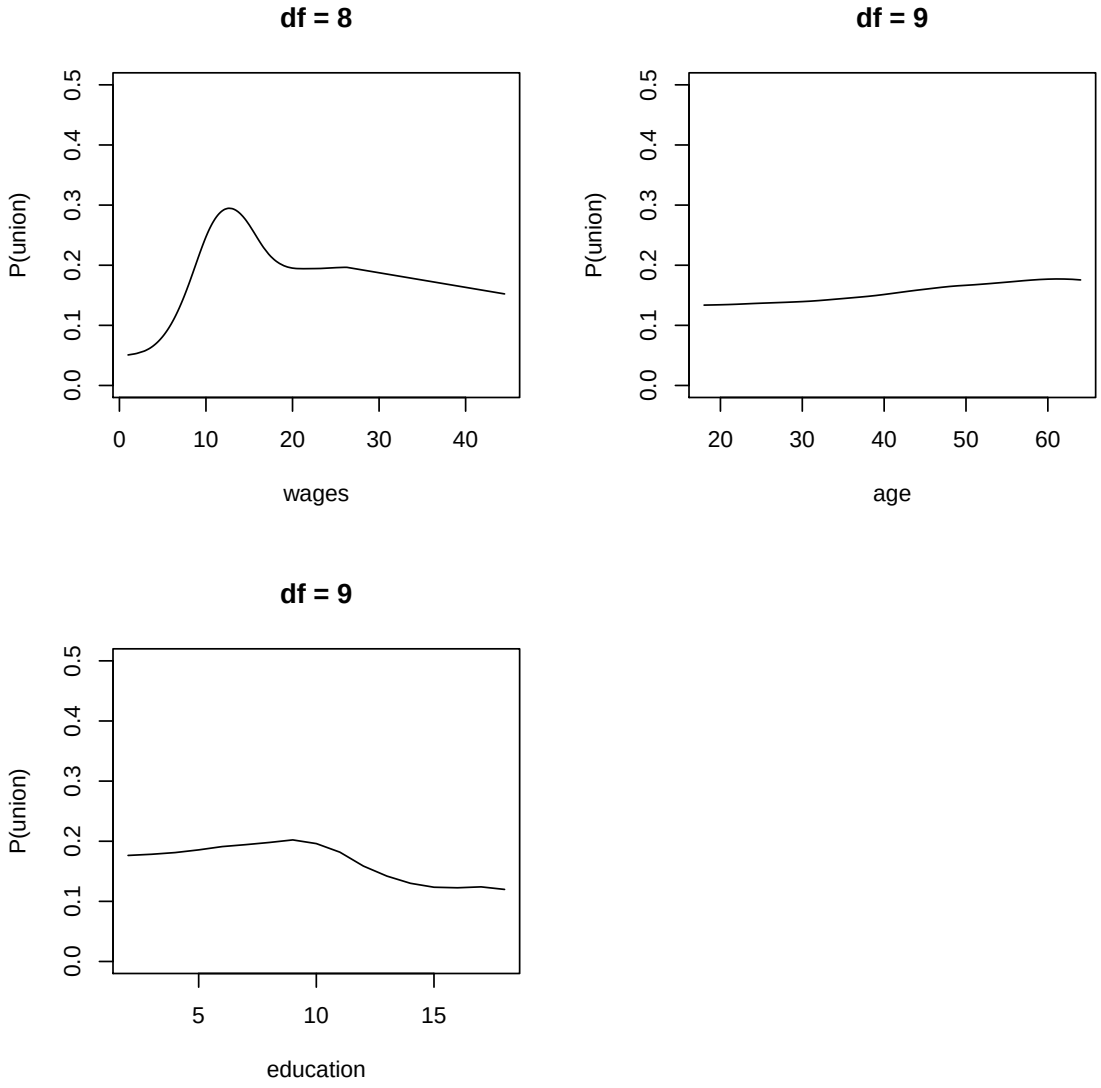


Figure A.1: Probablity of membership as a function of covariates. In each plot, the remaining covariates are fixed at their sample means. The effective degrees of freedom (df) are also given (Hastie & Tibshirani 1990).

The Wage-union data The data, which are available from Statlib (`lib.stat.cmu.edu/`), contain information for each of 534 workers about whether they are members ($y_i = 1$) of a workers union or not ($y_i = 0$). We study the probability of membership as a function of six covariates. Expressed in the notation used by the R (S-Plus) function `gam` the model is:

```
union ~race + sex + south + s(wage) + s(age) + s(ed), family=binomial
```

Here, `s()` denotes a spline functions with 20 knots each. For `wage` a cubic spline is used, while for `age` and `ed` quadratic splines are used. The total number of random effects that arrise from the three corresponding **u** vectors is 64. Figure A.1 shows the estimated nonparametric components of the model. The time taken to fit the model was 165 seconds.

Extentions

- The linear predictor may be a mix of ordinary regression terms ($f_j(x) = \beta_j x$) and nonparametric terms. ADMB-RE offers a unified approach to fitting such models, in which the smoothing parameters λ_j and the regression parameters β_j are estimated simultaneously.
- It is straight forward in ADMB-RE to add 'ordinary' random effects to the model, for instance to accomodate for correlation within groups of observations, as in Lin & Zhang (1999).

Files http://otter-rsch.com/admbre/examples/union/union.html

A.1.3 Semi-parametric estimation of mean and variance

Model description An assumption underlying the ordinary regression

$$y_i = a + bx_i + \varepsilon_i'$$

is that all observations have the same variance, i.e. $\mathrm{Var}(\varepsilon_i') = \sigma^2$. This assumption does not always hold, as for the data shown in the upper panel of Figure A.2. This example is taken from Ruppert et al. (2003).

It is clear that the variance increases to the right (for large values of x). It is also clear that the mean of y is not a linear function of x. We thus fit the model

$$y_i = f(x_i) + \sigma(x_i)\varepsilon_i,$$

where $\varepsilon_i \sim N(0,1)$, and $f(x)$ and $\sigma(x)$ are modelled nonparametrically. We take f to be a penalized spline. To ensure that $\sigma(x) > 0$ we model $\log[\sigma(x)]$, rather than $\sigma(x)$, as a spline function. For f we use a cubic spline (20 knots) with a 2nd order difference penalty

$$-\lambda^2 \sum_{k=3}^{20} \left(u_j - 2u_{j-1} + u_{j-2}\right)^2,$$

while we take $\log[\sigma(x)]$ to be a linear spline (20 knots) with the 1st order difference penalty (A.2).

Implementation details Details on how to implement spline components are given Example A.1.2.

- Parameter associated with f should be given 'phase 1' in ADMB, while those associated with σ should be given 'phase 2'. The reason is that in order to estimate the variation, one first needs to have fitted the mean part.

- In order to estimate the variation function, one first needs to have fitted the mean part. Parameter associated with f should thus be given 'phase 1' in ADMB, while those associated with σ should be given 'phase 2'.

Files http://otter-rsch.com/admbre/examples/lidar/lidar.html

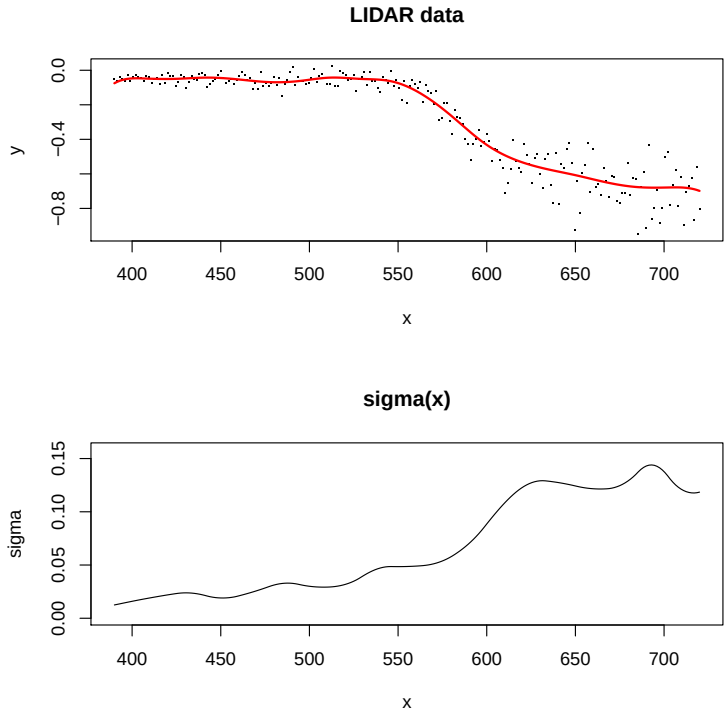


Figure A.2: LIDAR data (upper panel) used by Ruppert et al. (2003) with fitted mean. Fitted standard deviation is shown in the lower panel.

A.1.4 Weibull regression in survival analysis

Model description A typical setting in survival analysis is that we observe the time point t at which the death of a patient occurs. Patients may leave the study (for some reason) before they die. In this case the survival time is said to be censored, and t refers to the time point when the patient left the study. The indicator variable δ is used to indicate whether t refers to the death of the patient ($\delta = 1$) or to a censoring event ($\delta = 0$). The key quantity in modelling the probability distribution of t is the hazard function $h(t)$, which measures the instantaneous death rate at time t. We also define the cumulative hazard function $\Lambda(t) = \int_0^t h(s)ds$, implicitly assuming that the study started at time $t = 0$. The log likelihood contribution from our patient is $\delta \log(h(t)) - H(t)$. A commonly used model for $h(t)$ is Cox's proportional hazard model, in which the hazard rate for the ith patient is assumed to be on the form

$$h_i t = h_0(t) \exp(\eta_i), \qquad i = 1, \ldots n.$$

Here, $h_0(t)$ is the "baseline" hazard function (common to all patients) and $\eta_i = \mathbf{X}_i\beta$, where $\mathbf{X}_i$ is a covariate vector specific to the ith patient and β is a vector of regression parameters. In this example we shall assume that the baseline hazard belongs to the Weibull family: $h_0(t) = rt^{r-1}$ for $r > 0$.

In the collection of examples following the distribution of WinBUGS this model is used to analyse a dataset on times to kidney infection for a set of $n = 38$ patients (Kidney: Weibull regression with random effects, Examples Volume 1, WinBUGS 1.4). The dataset contains two observations per patient (the time to first and second recurrence of infection). In addition there are three covariates: *age* (continuous), *sex* (dichotomous) and *type of disease* (categorical, four levels), and an individual-specific random effect $u_i \sim N(0, \sigma^2)$. Thus, the linear predictor becomes

$$\eta_i = \beta_0 + \beta_{\text{sex}} \cdot \text{sex}_i + \beta_{\text{age}} \cdot \text{age}_i + \beta_{\text{D}}\, \mathbf{x}_i + u_i,$$

where $\beta_{\text{D}} = (\beta_1, \beta_2, \beta_3)$ and $\mathbf{x}_i$ is a dummy vector coding for the disease type. Parameter estimates are shown in the table below.

	β_0	β_{age}	β_1	β_2	β_3	β_{sex}	r	σ
ADMB-RE	-4.3440	0.0030	0.1208	0.6058	-1.1423	-1.8767	1.1624	0.5617
Std. dev.	0.8720	0.0137	0.5008	0.5011	0.7729	0.4754	0.1626	0.2970
BUGS	-4.6000	0.0030	0.1329	0.6444	-1.1680	-1.9380	1.2150	0.6374
Std. dev.	0.8962	0.0148	0.5393	0.5301	0.8335	0.4854	0.1623	0.3570

Files http://otter-rsch.com/admbre/examples/kidney/kidney.html

A.2 Block-diagonal Hessian

This section contains models with grouped or nested random effects

A.2.1 Nonlinear mixed models; a NLME comparison

Model description The orange tree growth data was used by Pinheiro & Bates (2000, Ch.8.2) to illustrate how a logistic growth curve model with random effects can be fit with the S-Plus function `nlme`. The data contain measurements made at seven occasions for each of five orange trees:

t_{ij}	Time point when the jth measurement was made on tree i
y_{ij}	Trunk circumference of tree i when measured at time point t_{ij}

The following logistic model is used:

$$y_{ij} = \frac{\phi_1 + u_i}{1 + \exp\left[-\left(t_{ij} - \phi_2\right)/\phi_3\right]} + \varepsilon_{ij},$$

where (ϕ_1, ϕ_2, ϕ_3) are hyper-parameters, and $u_i \sim N(0, \sigma_u^2)$ is a random effect, and $\varepsilon_{ij} \sim N(0, \sigma^2)$ is the residual noise term.

Results Parameter estimates are shown in the following table.

	ϕ_1	ϕ_2	ϕ_3	σ	σ_u
ADMB-RE	192.1	727.9	348.1	7.843	31.65
Std. dev.	15.658	35.249	27.08	1.013	10.26
`nlme`	191.0	722.6	344.2	7.846	31.48

The difference between the estimates obtained with ADMB-RE and `nlme` is small. The difference is caused by the fact that the two approaches use different approximations to the likelihood function. (ADMB-RE uses the Laplace approximation, and for `nlme` the reader is referred to (Pinheiro & Bates 2000, Ch. 7).)

The computation time for ADMB was 0.58 seconds, while the computation time for `nlme` (running under S-Plus 6.1) was 1.6 seconds.

Files http://otter-rsch.com/admbre/examples/orange/orange.html

A.2.2 Pharmacokinetics; a NLME comparison

Model description The 'one-compartment open model' is commonly used in pharmacokinetics. It can be described as follows. A patient receives a dose D of some substance at time t_d. The concentration c_t at a later time point t is governed by the equation

$$c_t = \frac{D}{V} \exp\left[-\frac{Cl}{V}(t - t_d)\right]$$

where V and Cl are parameters (the so-called 'Volume of concentration' and the 'Clearance'). Doses given at different time points contribute additively to c_t. Pinheiro & Bates (2000, Ch. 6.4) fitted this model to a dataset using the S-Plus routine `nlme`. The linear predictor used by Pinheiro & Bates (2000, p. 300) is:

$$\begin{aligned} \log(V) &= \beta_1 + \beta_2 Wt + u_V, \\ \log(Cl) &= \beta_3 + \beta_4 Wt + u_{Cl}, \end{aligned}$$

where Wt is a continuous covariate, and $u_V \sim N(0, \sigma_V^2)$ and $u_{Cl} \sim N(0, \sigma_{Cl}^2)$ are random effects. The model specification is completed by the requirement that the observed concentration y in the patient is related to the true concentration by $y = c_t + \varepsilon$, where $\varepsilon \sim N(0, \sigma^2)$ is a measurement error term.

Results Estimates of hyper-parameters are shown in the following table:

	β_1	β_2	β_3	β_4	σ	σ_V	σ_{Cl}
ADMB-RE	-5.99	0.622	-0.471	0.532	2.72	0.171	0.227
Std. Dev	0.13	0.076	0.067	0.040	0.23	0.024	0.054
`nlme`	-5.96	0.620	-0.485	0.532	2.73	0.173	0.216

The differences between the estimates obtained with ADMB-RE and `nlme` are caused by the fact that the two methods use different approximations of the likelihood function. ADMB-RE uses the Laplace approximation, while the method used by `nlme` is described in Pinheiro & Bates (2000, Ch. 7).

The time taken to fit the model by ADMB-RE was 17 seconds, while the computation time for `nlme` (under S-Plus 6.1) was 7 seconds.

Files http://otter-rsch.com/admbre/examples/pheno/pheno.html

A.2.3 Frequency weighting in ADMB-RE

Model description Let X_i be binomially distributed with paramters $N = 2$ and p_i, and assume that

$$p_i = \frac{\exp(\mu + u_i)}{1 + \exp(\mu + u_i)}, \tag{A.3}$$

where μ is a parameter and $u_i \sim N(0, \sigma^2)$ is a random effect. Assuming independe, the loglikelihood function for the parameter $\theta = (\mu, \sigma)$ can be written:

$$l(\theta) = \sum_{i=1}^{n} \log\left[p(x_i; \theta)\right]. \tag{A.4}$$

In ADMB-RE $p(x_i; \theta)$ is approximated using the Laplace approximation. However, since x_i only can take the values 0, 1 and 2, we can re-write the loglikelihood as

$$l(\theta) = \sum_{j=0}^{2} n_j \log\left[p(j; \theta)\right], \tag{A.5}$$

where n_j is the number x_i being equal to j. Still the Laplace approximation must be used to approximate $p(j; \theta)$, but now only for $j = 0, 1, 2$, as opposed to n times above. For large n this can give large savings.

To implement the loglikelihood (A.5) in ADMB-RE you must organize your code into a SEPARABLE_FUNCTION (see the section "Nested models" in the ADMB-RE manual). Then you should do the following

- Formulate the objective function in the weighted form (A.5).
- Include the statement `!! set_multinomial_weights(w)` in the PARAMTER_SECTION, where `w` is a vector (with indexes starting at 1) containg the weights, so in our case $w = (n_0, n_1, n_2)$.

Files http://otter-rsch.com/admbre/examples/weights/weights.html

A.2.4 Ordinal logistic regression

Model description In this model the response variable y takes on values from the ordered set $\{y^{(s)}, s = 1, \ldots, S-1\}$, where $y^{(1)} < y^{(2)} < \cdots < y^{(S)}$. For $s = 1, \ldots, S-1$ define $P_s = P(y \leq y^{(s)})$ and $\kappa_s = \log[P_s/(1-P_s)]$. To allow κ_s to depend on covariates specific to the ith observation $(i = 1, \ldots, n)$ we introduce a disturbance η_i of κ_s:

$$P(y_i \leq y^{(s)}) = \frac{\exp(\kappa_s - \eta_i)}{1 + \exp(\kappa_s - \eta_i)}, \qquad s = 1, \ldots, S-1.$$

with

$$\eta_i = \mathbf{X}_i \beta + u_{j_i},$$

where $\mathbf{X}_i$ and β play the sample role as in Example 1-3, the u_j $(j = 1, \ldots, q)$ are independent $N(0, \sigma^2)$ variables, and j_i is the latent variable class of individual i.

Files http://otter-rsch.com/admbre/examples/socatt/socatt.html

A.3 Banded Hessian (state-space)

Examples of state-space models.

A.3.1 Stochastic volatility models in finance

Model description Stochastic volatility models are used in mathematical finance to describe the evolution of asset returns, which typically exhibit changing variances over time. As an illustration we use a time series of daily pound/-dollar exchange rates $\{z_t\}$ from the period 01/10/81 to 28/6/85, previously analyzed by Harvey, Ruiz & Shephard (1994). The series of interest are the daily mean-corrected returns $\{y_t\}$, given by the transformation

$$y_t = \log z_t - \log z_{t-1} - n^{-1} \sum_{i=1}^{n} (\log z_t - \log z_{t-1}).$$

The stochastic volatility model allows the variance of y_t to vary smoothly with time. This is achieved by assuming that $yt \sim N(\mu, \sigma_t^2)$, where $\sigma_t^2 = \exp(\mu_x + x_t)$. The smoothly varying component x_t follows the autoregression

$$x_t = \beta x_{t-1} + \varepsilon_t, \qquad \varepsilon_t \sim N(0, \sigma^2).$$

The vector of hyper-parameters is for this model is thus $(\beta, \sigma, \mu, \mu_x)$.

Files http://otter-rsch.com/admbre/examples/sdv/sdv.html

A.3.2 A discrete valued time series; The polio dataset

Model description Zeger (1988) analyzed a time series of monthly numbers of poliomyelitis cases during the period 1970–1983 in the US. We make comparison to the performance of the Monte Carlo Newton-Raphson method as reported in Kuk & Cheng (1999). We adopt their model formulation.

Let y_i denote the number of polio cases in the ith period ($i = 1, \ldots, 168$). It is assumed that the distribution of y_i is governed by a latent stationary AR(1) process $\{u_i\}$ satisfying

$$u_i = \rho u_{i-1} + \varepsilon_i,$$

where the $\varepsilon_i \sim N(0, \sigma^2)$ variables. To account for trend and seasonality the following covariate vector is introduced

$$\mathbf{x}_i = \left(1, \frac{i}{1000}, \cos\left(\frac{2\pi}{12}i\right), \sin\left(\frac{2\pi}{12}i\right), \cos\left(\frac{2\pi}{6}i\right), \sin\left(\frac{2\pi}{6}i\right)\right).$$

Conditionally on the latent process $\{u_i\}$, the counts y_i are independently Poisson distributed with intensity

$$\lambda_i = \exp(\mathbf{x}_i{}'\beta + u_i).$$

Conditionally on the latent process $\{u_i\}$, the counts y_i are independently Poisson distributed with intensity

$$\lambda_i = \exp(\mathbf{x}_i{}'\beta + u_i).$$

Results Estimates of hyper-parameters are shown in the following table.

	β_1	β_2	β_3	β_4	β_5	β_6	ρ	σ
ADMB-RE	0.242	-3.81	0.162	-0.482	0.413	-0.0109	0.627	0.538
Std. dev.	0.270	2.76	0.150	0.160	0.130	0.1300	0.190	0.150
Kuk & Cheng (1999)	0.244	-3.82	0.162	-0.478	0.413	-0.0109	0.665	0.519

We note that not the standard deviation is large for several regression parameters. The ADMB-RE estimates (which are based on the Laplace approximation) very are very similar to the exact maximum likelihood estimates as obtained with the method of Kuk & Cheng (1999).

Files http://otter-rsch.com/admbre/examples/polio/polio.html

A.4 Generally sparse Hessian

A.4.1 Multilevel Rasch model

The multilevel Rasch model can be implented using random effects in ADMB. As an example we use data on the responses of 2042 soldiers to a total of 19 items (questions), taken from Doran et al (2007). This illustrates the use of crossed random effects in ADMB. Further, it is shown how the model easily can be generalized in ADMB. These more general models cannot be fitted with standard GLMM software such as "lmer" in R.

Files http://admb-project.org/community/tutorials-and-examples/ random-effects-example-collection/item-response-theory-irt-and-the-multilevel-rasch-model-1

Appendix B

Which ADMB features are not in ADMB-RE

- Profile likelihoods cannot be used.
- Certain functions, especially for matrix operations, have not been implemented.

You will find that not all the functionality of ordinary ADMB has yet been implemented in ADMB-RE. Functions are being added all the time.

Appendix C

Command line options

A list of command line options accepted by ADMB programs can be obtained using the command line option `-?`, for instance

```
$ simple -?
```

Those options that are specific to ADMB-RE are printed after line the "Random effects options if applicable":

Option	Explanation
`-nr N`	maximum number of Newton-Raphson steps
`-imaxfn N`	maximum number of fevals in quasi-Newton inner optimization
`-is N`	set importance sampling size to n for random effects
`-isf N`	set importance sampling size funnel blocksto n for random effects
`-isdiag`	print importance sampling diagnostics
`-hybrid`	do hybrid Monte Carlo version of MCMC
`-hbf`	set the hybrid bounded flag for bounded parameters
`-hyeps`	mean step size for hybrid Monte Carlo
`-hynstep`	number of steps for hybrid Monte Carlo
`-noinit`	do not initialize random effects before inner optimzation
`-ndi N`	set maximum number of separable calls
`-ndb N`	set number of blocks for derivatives for random effects (reduces temporary file sizes)
`-ddnr`	use high precision Newton-Raphson for inner optimization for banded hessian case ONI
`-nrdbg`	verbose reporting for debugging newton-raphson
`-mm N`	do minimax optimization
`-shess`	use sparse Hessian structure inner optimzation
`-l1 N`	set the size of buffer `f1b2list1` to `N`
`-l2 N`	set the size of buffer `f1b2list12` to `N`
`-l3 N`	set the size of buffer `f1b2list13` to `N`
`-nl1 N`	set the size of buffer `nf1b2list1` to `N`
`-nl2 N`	set the size of buffer `nf1b2list12` to `N`
`-nl3 N`	set the size of buffer `nf1b2list13` to `N`

The last section (following the horisontal bar) are not printed, but can still be used (se earlier).

Appendix D

Quick references

D.1 Compiling ADMB programs

To compile `model.tpl` in a DOS/Linux terminal window:

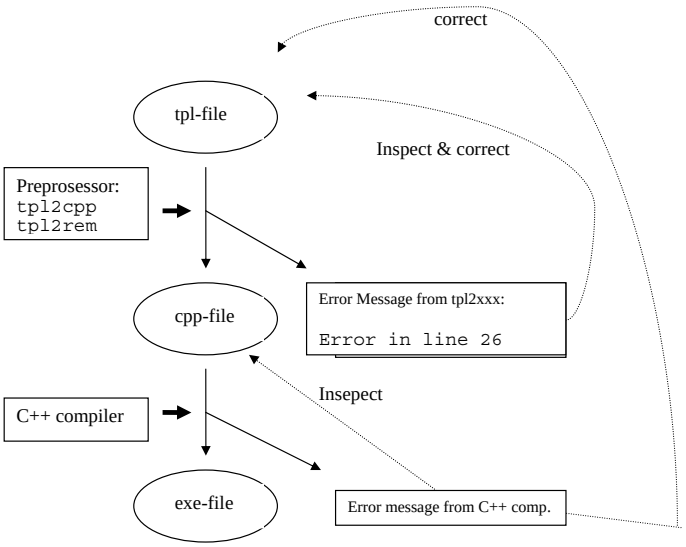
```
admb [-s] [-r] model
```

where the options
`-s` yields the "safe" version of the exe-file
`-r` is used to invoke the random effect module

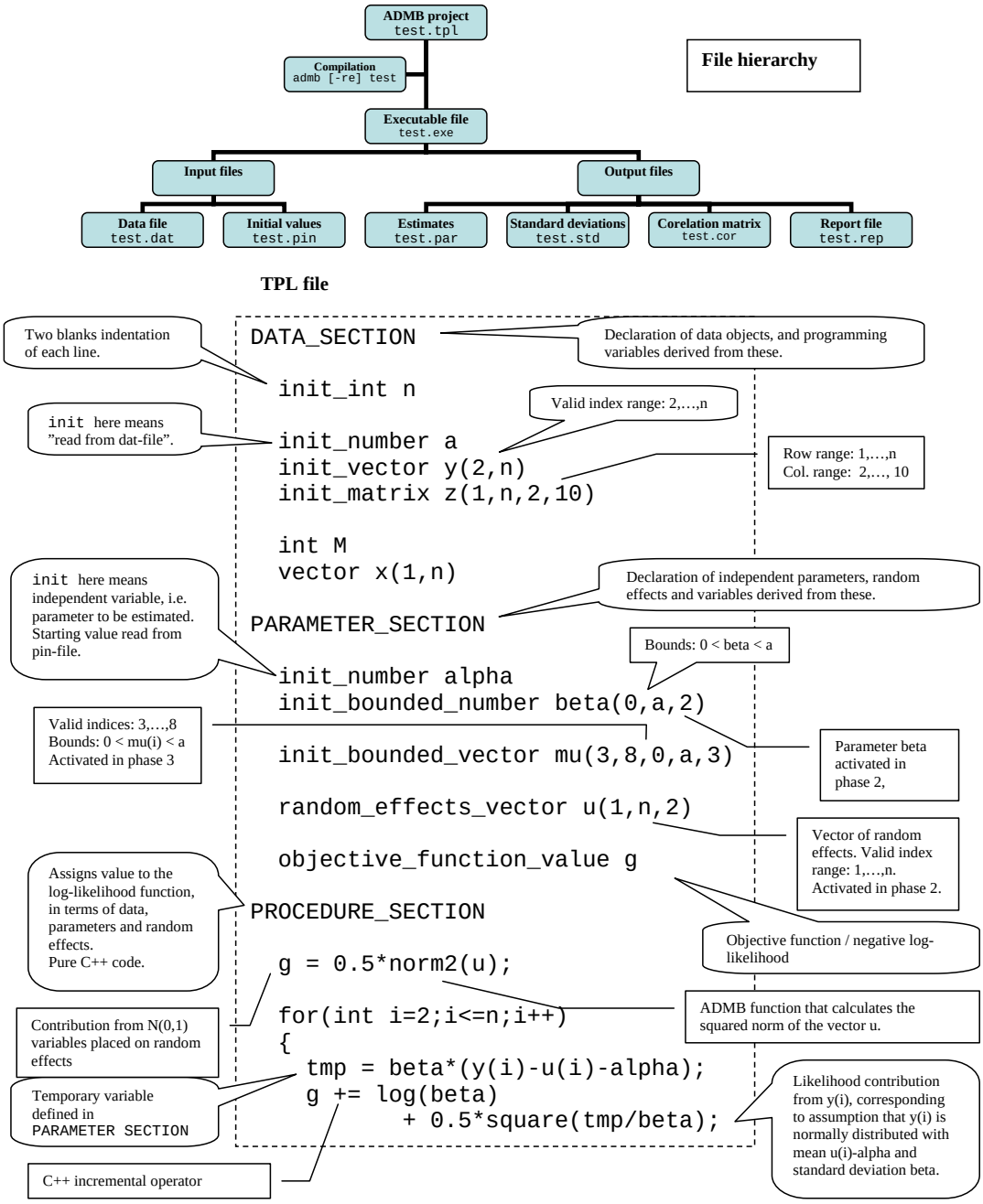
Two stages of compilation:
1. Preprosessor: `tpl2cpp` or `tpl2rem` (ADMB-RE)
2. C++ compiler (Borland, Visual C++, gcc, etc.) with two stages:
   - Compilation: `adcomp`
   - Linking: `adlink`

Location of all scripts/functions: `%ADMB_HOME%\bin`
- `ADMB_HOME` is the environment variable pointing to the home directory of the ADMB installation

Illustration of compilation process (nicely integrated in the ADMB-IDE)



D.2


The ADMB primer
ADMB project
test.tpl
Compilation
admb [-re] test
Executable file
test.exe
File hierarchy
Input files
Output files
Data file
test.dat
Initial values
test.pin
Estimates
test.par
Standard deviations
test.std
Corelation matrix
test.cor
Report file
test.rep
TPL file
Two blanks indentation of each line.
DATA_SECTION
Declaration of data objects, and programming variables derived from these.
init_int n
init here means "read from dat-file".
Valid index range: 2,…,n
init_number a
init_vector y(2,n)
Row range: 1,…,n
Col. range: 2,…, 10
init_matrix z(1,n,2,10)
int M
vector x(1,n)
init here means independent variable, i.e. parameter to be estimated. Starting value read from pin-file.
Declaration of independent parameters, random effects and variables derived from these.
PARAMETER_SECTION
Bounds: 0 < beta < a
init_number alpha
init_bounded_number beta(0,a,2)
Valid indices: 3,…,8
Bounds: 0 < mu(i) < a
Activated in phase 3
Parameter beta activated in phase 2,
init_bounded_vector mu(3,8,0,a,3)
random_effects_vector u(1,n,2)
Vector of random effects. Valid index range: 1,…,n. Activated in phase 2.
objective_function_value g
Assigns value to the log-likelihood function, in terms of data, parameters and random effects. Pure C++ code.
PROCEDURE_SECTION
Objective function / negative log-likelihood
g = 0.5*norm2(u);
ADMB function that calculates the squared norm of the vector u.
Contribution from N(0,1) variables placed on random effects
for(int i=2;i<=n;i++)
{
tmp = beta*(y(i)-u(i)-alpha);
Temporary variable defined in PARAMETER SECTION
g += log(beta)
+ 0.5*square(tmp/beta);
Likelihood contribution from y(i), corresponding to assumption that y(i) is normally distributed with mean u(i)-alpha and standard deviation beta.
C++ incremental operator

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