

---

# MiX99

**Solving Large Mixed Model Equations**

---

Release VIII/2015

**TECHNICAL REFERENCE GUIDE  
FOR  
MiX99 SOLVER**

## Preface

Development of MiX99 was initiated to allow analysis of sophisticated linear mixed models in estimation of breeding values for dairy cattle. In the first versions, the emphasis was on computational efficiency and the target users were experts on genetic evaluations. Therefore, logic in defining the model was from animal breeding perspective. The foremost application of this software is solving of large random regression test-day models for national dairy cattle evaluations. Nevertheless, our goal has been to keep the software as a general tool, which allows analysing different kind of linear mixed models. As a result, besides cattle, MiX99 is used in genetic evaluation of other species like pig, horse, sheep, fish, fox, poultry, and for many types of research work.

## Disclaimer

MiX99 software is owned by Biometrical Genetics at Natural Resources Institute Finland (Luke). When using this program you agree with the following terms. You are not allowed to distribute, copy, give or transfer MiX99, neither under the same nor under a different name. Any decisions based on information given by MiX99 are made at your own responsibility and risk. Only limited technical support can be provided, but vital questions on its use can be directed to the authors ([firstname.lastname@luke.fi](mailto:firstname.lastname@luke.fi)). Please report any bugs to the authors. MiX99 can be referenced by ([MiX99 Development Team, 2015](#)). If you would like to use MiX99, please contact Biometrical Genetics at Natural Resources Institute Finland<sup>1</sup>.

## Authors

Martin Lidauer, Kaarina Matilainen, Esa Mäntysaari, Timo Pitkänen, Matti Taskinen, Ismo Strandén

Biometrical Genetics,  
Green Technology,  
Natural Resources Institute Finland (Luke),  
FI-31600 Jokioinen, Finland  
[firstname.lastname@luke.fi](mailto:firstname.lastname@luke.fi)  
<http://www.luke.fi/mix99>

---

<sup>1</sup>MiX99 Development Team, Biometrical Genetics, Natural Resources Institute Finland (Luke), FI-31600 Jokioinen, Finland.

# Contents

1	Introduction . . . . .	1
2	Computing Methods . . . . .	2
2.1	Preconditioned conjugate gradient method . . . . .	2
2.2	Iteration on data technique . . . . .	2
2.3	Data work file reduction . . . . .	2
2.4	Equation family blocks . . . . .	3
3	How to run MiX99 solver programs . . . . .	4
3.1	Computing environment . . . . .	4
3.2	Programs and compiling . . . . .	4
3.3	Running the solver . . . . .	4
4	The MiX99 solver option file . . . . .	6
4.1	Solver option lines . . . . .	6
4.2	Determining convergence . . . . .	13
4.2.1	Choosing a suitable convergence criteria . . . . .	14
4.2.2	Effect of preconditioning on convergence . . . . .	14
4.3	External STOP . . . . .	15
5	Output files of the MiX99 solvers . . . . .	17
5.1	Standard output . . . . .	17
5.2	Solution files . . . . .	17
5.2.1	Formatted solution files . . . . .	17
5.2.2	Unformatted solution files . . . . .	17
5.3	Files for model validation purposes . . . . .	18
6	Reliabilities . . . . .	20
6.1	Approximate reliabilities using ApaX . . . . .	20
6.1.1	Differences of reliability calculation and breeding value estimation . . . . .	21
6.1.2	ApaX instruction file . . . . .	21
6.1.3	Guidelines for determining blocking and JFilter . . . . .	24
6.1.4	ApaX Output files . . . . .	26
6.1.5	Example of ApaX instruction file . . . . .	26
6.2	Exact reliabilities using exa99 . . . . .	29
6.2.1	Option file for exa99 . . . . .	29
6.2.2	Exa99 output files . . . . .	29
6.3	Reversed reliability approximation . . . . .	30
7	Daughter Yield Deviations . . . . .	32
7.1	Calculation of daughter yield deviations . . . . .	32
7.1.1	Pedigree file . . . . .	32
7.1.2	MiX99 instruction file . . . . .	32

# TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

7.1.3	MiX99 solver option file . . . . .	33
7.2	Solution files for daughter yield deviations . . . . .	33
7.3	Example . . . . .	33
8	Non-linear models . . . . .	36
8.1	Threshold-model . . . . .	36
8.1.1	Instruction file for <i>mix99i</i> . . . . .	36
8.1.2	Stopping criteria file for <i>mix99s</i> . . . . .	36
8.1.3	Solution files . . . . .	37
8.1.4	Example . . . . .	37
8.2	Gompertz-model . . . . .	37
8.2.1	Instruction file for <i>mix99i</i> . . . . .	37
8.2.2	Stopping criteria file for <i>mix99s</i> . . . . .	38
8.2.3	Solution files . . . . .	38
8.2.4	Example . . . . .	39
9	Estimation of variance components . . . . .	40
9.1	File with (co)variance components starting values (PARFILE) . . . . .	40
9.2	MiX99 instruction file . . . . .	40
9.3	MiX99 solver option file . . . . .	41
9.3.1	Keeping certain variance components fixed . . . . .	41
9.4	Determining convergence of REML parameter estimates . . . . .	42
9.5	Standard errors for REML parameter estimates . . . . .	42
9.6	Solution files for variance components . . . . .	44
9.7	Example . . . . .	45
10	Accounting for heterogeneous variance . . . . .	48
10.1	Computation environment . . . . .	48
10.2	Models for the heterogeneity of variances . . . . .	48
10.2.1	Currently supported <i>variance models</i> by MiX99 . . . . .	48
10.3	Input data for the variance model . . . . .	51
10.3.1	Input data for <i>mix99hv</i> . . . . .	51
10.3.2	Instruction file for <i>mix99hv</i> . . . . .	51
10.3.3	Output files from <i>mix99hv</i> . . . . .	53
10.4	Instruction file for the variance model . . . . .	54
10.5	Variance components for the variance model . . . . .	57
10.5.1	Files with information for the variance component estimation . . . . .	57
10.6	Standardization of the multiplicative adjustment factors . . . . .	58
10.6.1	Files for the standardization procedure . . . . .	58
10.6.2	Standardization process . . . . .	59
10.6.3	Multiple residual variance-covariance matrices . . . . .	59
10.7	Running a model with heterogeneous variance . . . . .	60
10.7.1	Implementation on shared memory platforms . . . . .	60
10.8	Workflow and needed files for running multiplicative mixed model . . . . .	61
10.9	Example . . . . .	63
10.10	Output files . . . . .	65
10.10.1	Mi.log and Ms.log . . . . .	65
10.10.2	HVd.log . . . . .	66
10.10.3	CYC.log . . . . .	66
10.10.4	Lambda.log . . . . .	67

# TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

11	Acknowledgement	68
12	References	68
	Index	71

# 1 Introduction

Dairy cattle breeders around the world have moved to so called test-day models from plain animal models for 305d data. Usually this model upgrade leads to a manifold increase in computations. This is because test-day models have more effects than traditional models based on 305d data, and also because number of records increase about ten times. In a national evaluation, number of test-day records and number of unknowns in the mixed model equations (MME) are easily more than 100 million.

Computational techniques and algorithms that were found useful for solving animal models may take weeks to obtain solution to large random regression test day model MME. Consequently, faster solving algorithms had to be developed. [Strandén and Lidauer \(1999\)](#) and [Lidauer et al. \(1999\)](#) advocated the use of [preconditioned conjugate gradient \(PCG\) method](#). [Lidauer and Strandén \(1998\)](#) and [Strandén \(1999\)](#) showed the usefulness of [parallel computing](#). These techniques have been found to reduce computing time considerably.

MiX99 development work focused on incorporation of these new techniques into an iteration on data BLUP-program ([Lidauer and Strandén, 1999](#)). We have also extended the software with programs for different needs: a general program that [approximate reliabilities](#) of bulls' estimated breeding values (EBV), as required by the Interbull; a general program that calculates [exact reliabilities](#) of EBVs via inversion of the coefficient matrix; and programs, which are required when accounting for [heterogeneous variance](#). Although the programs have been designed primarily for genetic evaluation of dairy cattle, the programs can and are used for other species that use other types of statistical models.

The MiX99 package consists of two main programs: pre-processor and solver. The pre-processor program `mix99i` reads model instructions, examines input data, and computes data sets for the solver program `mix99s`, which solves the MME by [iteration on data](#). The MME can also be solved by the program `mix99p`, which is designed to use several CPUs in [parallel](#). In addition, the pre-processed data can be analysed with additional programs (`apax99`, `apax99p` and `exa99`) to compute accuracies of the breeding values. For giving instructions to `mix99i` please see the manuals [Command Language Interface for MiX99](#) and [Technical reference guide for MiX99 pre-processor](#). In this reference guide we describe the solver options and instructions for `mix99s`, `mix99p`, `apax99`, `apax99p`, and `exa99`.

## 2 Computing Methods

### 2.1 Preconditioned conjugate gradient method

The method of conjugate gradient (CG) is an iterative method to solve a linear system  $\mathbf{Cs}=\mathbf{r}$ . It is based on a geometric approach (Shewchuk, 1994). In breeding value estimation, the  $\mathbf{C}$  matrix corresponds to the coefficient matrix of mixed model equations (MME), the  $\mathbf{s}$  vector contains the solutions, and the  $\mathbf{r}$  vector is the right-hand side of MME.

Preconditioned conjugate gradient method (PCG) uses conjugate gradient method on a transformed problem. Preconditioning is equivalent to solving  $\mathbf{M}^{-1}\mathbf{Cs} = \mathbf{M}^{-1}\mathbf{r}$ , where  $\mathbf{M}$  is a symmetric positive definite preconditioner matrix that approximates  $\mathbf{C}$ . Together with a suitable preconditioner matrix, convergence rate of the CG method is superior to other commonly used algorithms for solving MME (Lidauer et al., 1999).

MiX99 program creates the preconditioner matrix  $\mathbf{M}$ , which comprises of diagonal blocks of the coefficient matrix. Implementation of the PCG algorithm using iteration on data (IOD) technique requires keeping four vectors, of size equal to the number of unknowns in the MME, in memory and to read the data and the preconditioner matrix once per iteration round. The algorithm does not require any pre-set tuning parameters like relaxation factors.

### 2.2 Iteration on data technique

The major computational task in PCG is the multiplication of the coefficient matrix with a vector each round of iteration. Therefore, in IOD all data records must be read and processed. IOD technique requires for each record a certain amount ( $N$ ) of floating point operations to calculate the product coefficient matrix times a vector corresponding to the record. In MiX99,  $N$  increases almost linearly with increasing complexity of the statistical model;  $N=2(2f+t^2)$ , where  $f$  is the number of effects in the model, and  $t$  is the number of traits in the model.

### 2.3 Data work file reduction

Complex models with many effects may yield large iteration work files, which increases disk input/output (I/O) work. Iteration work files were made smaller by a data reduction technique. Data file reduction in MiX99 is based on the concept of avoiding redundant information. The following strategies were considered useful when complex statistical models were used for a typical dairy cattle data:

- 1) Pedigree information and observation data are stored in separate files.
- 2) If several effects in the model have the same class code, only one equation identification number is stored in the iteration data file. This is possible by properly ordering the equations. For example, all random effects on animal like additive genetic and none-additive environment effect have the same class code.
- 3) All regression covariables or a part of them may be placed in a small table rather than read from the data file. The table is accessed by an index. For example, functions of days in milk can be put to a table and the connected covariate values are found by days in milk index.

- 4) When different traits are measured at different time (e.g. different lactation), observations of the traits may be grouped by the time component to avoid storing large amount of dummy variables for missing information.

## 2.4 Equation family blocks

In MiX99, equations are ordered by equation families. An equation family block comprises of closely linked equations in the MME. For example in dairy cattle fixed and random effects that belong to the same herd (herd test-day effects, cows' non-genetic and genetic effects, etc.) are closely linked to each other and therefore form a block of equations. Equations of fixed and random effects which are present in different herds, e.g. age effect or sire effect, are combined into common blocks. The equation family order increases data locality in the computations, which enhances computing speed, and is essential when using [parallel computing](#) (Strandén and Lidauer, 1999). For more information see [equation family](#) blocks in the *Technical reference guide for MiX99 pre-processor*.

## 3 How to run MiX99 solver programs

### 3.1 Computing environment

MiX99 is written in standard Fortran 90 and is self-contained. It is developed in UNIX and Linux environment. The program has been tested to compile under many UNIX and Linux Fortran 90/95 compilers as well as Windows compilers. When [parallel computing](#) is used, a Message Passing Interface (MPI) library must be available. For the development of the parallel processing code the Message Passing Interface library MPICH was used (<http://www.mcs.anl.gov/mpi/>).

### 3.2 Programs and compiling

Executing the MiX99 pre-processor program `mix99i` (see [Technical reference guide for MiX99 pre-processor](#)) will create all necessary files for the solver programs. There is a single processor and a parallel processor program available for solving the MME. Both programs use [iteration on data](#) technique and solve the MME by the [PCG](#) method:

- mix99s** Uses one processor for solving. During the iteration process it reads the work files `Tmp4.pedi0`, `Tmp5.clas0`, `Tmp6.diab0`, and `Tm10.trco0` every round of iteration. After convergence, final solutions are written to solution files.
- mix99p** Uses several processors in parallel for solving. Number of [parallel](#) processes, i.e., processors if available, is defined in the MiX99 [instruction file](#) for `mix99i`. An additional pre-processing program, named `imake99` needs to be executed before running `mix99p`. The `imake99` program makes a file called `Index.bin`. During the iteration, each process (i) reads its own [work files](#) `Tmp4.pedi(i)`, `Tmp5.clas(i)`, `Tmp6.diab(i)`, and `Tm10.trco(i)` every round of iteration. After convergence, one process writes the final solution to the solution files.

Before executing the above listed programs, they must be compiled. Compiler optimization options may be used to increase execution speed of the programs. We recommend the basic optimization option `-O`, but you might get faster executable code with some other optimization level. However, the subroutines in the `dlamch.f90` file, used by `mix99s`, must be compiled without optimization. Note, `mix99p` memory allocation is fully dynamic in MiX99 versions XI-2010 and higher and needs to be compiled only once at the [parallel computing](#) platform.

### 3.3 Running the solver

Solving mixed model equations using MiX99 involves execution of at least two programs. First, the pre-processing program `mix99i` is executed. In order to execute this program, two alternatives about how to give model information are available: either by providing a CLIM command file on the command line or by directing a MiX99 instruction file to the standard input (see [Command Language Interface for MiX99](#); [Technical reference guide for MiX99 pre-processor](#)). After this pre-processing step, the solver program `mix99s` is executed. The solver reads a [solver option file](#) from the standard

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

input. Both programs write information about the data to be analyzed, the model, information about the iteration process, part of solutions, etc. to standard output. The most important information about the analysis is written to the `MiX99.lst` file:

### Execution alternative 1:

```
1  mix99i CLIM_command_file
2
3  mix99s < solver_option_file
```

### Execution alternative 2:

```
1  mix99i < MiX99_instruction_file
2
3  mix99s < solver_option_file
```

When [parallel computing](#) is used, instead of executing `mix99s` you have to execute `imake99` and `mix99p` after the `mix99i` run has finished:

```
1  imake99
2
3  mpiexec99 -np 4 mix99p < solver_option_file
```

## 4 The MiX99 solver option file

The solvers `mix99s` and `mix99p` can be instructed with different parameters to control memory use, the iteration process, the solving of non-linear models (threshold models, multiplicative models for [heterogeneous variance adjustment](#)); to advise `mix99s` to estimate variance components; or to give instruction to the solver programs to calculate [yield deviations](#), [residuals](#), etc. The solver options must be provided by a solver option file, which is read by the programs from standard input. The **MiX99 solver option files** in the provided examples are named with the suffix `.slv`. However, any name can be given.

### Example of MiX99 solver option file:

```

1 # RAM: RAM demand: H=high, M=medium, L=low
2   H
3 # STOP: Max. num. iterations, Stopping criterion, Convergence indicator, enforce
4   5000          5.0e-5          d          f
5 # RESID: Calculate residuals? (Y/N)
6   N
7 # VALID: N=none, P=prediction, S=sum of effects, Y=YD, D=DYD, I=IDD
8   N
9 # VAROPT: adjust for heterogeneous variance / variance components: (N, E, S, C)
10  N
11 # SOLTYP: type of solution files? (Y,N,A,H)
12  Y
    
```

### 4.1 Solver option lines

The MiX99 [solver option file](#) consists of option lines asked by the program. There can be several option lines. The order of the option lines must be the same as given in the following. Option lines are not obligatory. However, if one of the option lines is left away all succeeding lines must be left away as well. The solver programs will use default values in case an empty MiX99 [solver option file](#) is provided or if a part of the option lines are not specified. The solver option file can contain comment lines in the same manner as in the MiX99 [instruction file](#). Information specified after the character `#` are considered as comments. Options specified by characters can be given either in upper case or in low case characters.

**RAM** A line with one character, which defines the use of random access memory.

**h High.** All required vectors are kept in memory (fastest execution time).

**m Medium.** Solutions are stored on the disk.

**l Low.** Solutions and [residuals](#) are stored on the disk.

The option **m** and **l** will reduce memory requirements by 25% and 50%, respectively, with the penalty to increase I/O-operations. However, in case of memory limitations, the option **m** and **l** may yield shortest execution time.

**Default value:** h.

**STOP** One line with three (`mix99p`) or four (`mix99s`) entries:

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

```
1 # maxiter, tolerance, criteria (A/R/D), [enforce (F)]:  
2 5000 5.0e-5 D F
```

The first entry is an integer number that specifies the **maximum number of iterations**. The second entry is a real value that specifies the **stopping criterion**. The third entry is a character that specifies the **convergence indicator** to which the stopping criterion will be applied. For example, if a character **a** is specified, then the iteration process will continue until the convergence indicator **CA** will reach a value smaller than the stopping criterion that is specified on entry two. The solver programs provide three types of convergence indicators. A definition of the convergence indicators is given in point 4.2:

- a CA.** Relative difference between right-hand and left-hand side of the MME considering all equations of the additive genetic animal effects only. If CA is defined, a suitable stopping criterion could be 1.0e-4 or 1.0e-5. However, the value is model-dependent and should be at least as small as needed to ensure that the **CD** convergence indicator reaches a value of 1.0.e-4.
- r CR.** Relative difference between right-hand and left-hand side of the MME considering all equations.
- d CD.** Relative difference between solutions of the last two iteration rounds. If CD is defined, a suitable stopping criterion for the majority of analyses would be 1.0e-4. For some multiple trait models and for [estimation of variance components](#) it was found that the criterion should be stricter (5.0e-5).

The fourth entry is optional and is needed for the **mix99s** solver only. The **mix99s** solver will consider the **STOP** option line only in case an enforcing character **f** is specified for the fourth entry. Otherwise default values will be used.

### **Default values for mix99s: 5000 1.0e-4 d**

In case of solving a [threshold-model](#), a non-linear model will be solved and the iteration process works on two different levels. Therefore, for a threshold-model the **STOP** line must have five entries: an integer, a real value, a character, an enforcing character **f**, and one additional integer. Now the first integer value gives the maximum number of **PCG**-iterations within each NR- or EM-round (default is 100 or number of equations in the MME) and the last integer value gives the maximum number of NR- or EM-rounds (default is 5000).

## **RESID**

A line with one character specifying the calculation of [residuals](#).

- y Yes.** [Residuals](#) will be written into the file(s) `eHat.data(i)`. When using the single processor solver **mix99s**, (i) will be zero (0). In case of [parallel processing](#), each process writes an own `eHat.data(i)` file with the process number (i) at the end of the file name. The order of the [residuals](#) corresponds with the order of observations in the input data file. In case of [parallel processing](#), the order of the residual files corresponds to the order of observations in the input data file

beginning with file zero (0) up to number of processes minus one. The `eHat.data(i)` files have as many columns with **residuals** as the maximum number of traits in the largest trait group. This is equal to the `mxntra` parameter given in the `Parlog` file. The `Parlog` file is produced by `mix99i`. The residual columns are ordered in the same sequence as the traits in the trait groups. For missing observations the corresponding value in the residual files are set to the **missing value -8192.0**.

- n** **No.** No **residuals** are written.
- h** This option is only available in `mix99p` and will create the file(s) `ARsiwi.data(i)`, which contain information about the heterogeneity of variance in the residuals. These files are needed only when accounting for **heterogeneous variance** (see chapter **Accounting for heterogeneous variance**).

**Default value: n**

**VALID**

A line with one entry, which instructs the solver to calculate for each observation a corresponding, here specified, sub-quantity of the applied model line, or to instruct the solver to simulate observations based on the specified model. The calculated quantities are written to binary files after the iteration process has ended. **Missing values** will be specified with **-8192.0**. The structure of the files will be explained in the chapter 5:

- n** **None.** None of the options are requested.
- p** **Predictions.** For each observations the predicted value ( $\hat{y}$ ) is written to the file(s) `yHat.data(i)`.
- s** **Selected Model Factors' Sum.** For each observation the sum of selected model factors is written to the file(s) `sHat.data(i)`. The selected factors must be specified on a following line.
- y** **Yield Deviations (YD).** For each observation the corresponding YD will be written to the file(s) named `YD.data(i)`. The factors included into the YD must be specified on a following line.
- i** **Individual Daughter Deviations (IDD).** For each observation the corresponding IDD will be written into the file(s) named `IDD.data(i)`. The factors included into the IDD must be specified on a following line.
- d** **Daughter Yield Deviations (DYD).** The solver will calculate for each observation the corresponding IDD and will use it for the calculation of DYDs based on the approach of **Mrode and Swanson (2004)**. For this option the calculated DYD will be written to a formatted file named `Soldyd`. (see chapter **Calculation of daughter yield deviations**). The factors included into the DYD must be specified on a following line.
- g** **Generate Observations.** This option is available in `mix99s` only. The `mix99s` solver will not solve the model, but instead will generate for each observation in the data a simulated observation ( $\hat{y}$ ). Therefore, for all effects in the model true solutions will be simulated based on the provided variance components. Fixed effect solutions

will be set to zero. The true solutions are written to the **MiX99** standard solution files. The generated observations will be written into the file named `ySim.data0`. This file can be used in a future **MiX99** run to replace real observation by simulated observations. See the **VAR** instruction line in the *Technical reference guide for MiX99 pre-processor* for reading and using of the generated observations instead of the real observations.

When specifying **g** a **SEED** option line must be included after the **VAROPT** option line. The **SEED** option line has one entry, which must be one of those given in the **SEED** option description below (see **VAROPT**).

- r **Deregression.** (See chapter: “Deregression” in *Command Language Interface for MiX99*).

The options **y**, **i**, **d** and **g** are not supported when solving non-linear models.

The options **s**, **y**, **i**, or **d** will require adding of a second line, which specifies which factors of the model are included into the calculation of the specified quantity.

**FACTOR** One line with as many integers as there are factor columns defined in the **REGRESS** instruction line. This is equal to the first integer value of the **REGRESS** instruction line (see *Technical reference guide for MiX99 pre-processor*). The order of the integer values on the **FACTOR** line corresponds to the order of the factors specified on the **REGRESS** instruction line. Each integer specifies whether or not the corresponding factor of the model is included into the calculation of the desired quantity.

- 1 The factor will be included into the specified quantity
- 0 The factor will be excluded from the specified quantity

**Specification of the factors for the desired quantities will be as following:**

Let's assume a model, for which the solver will have the following model terms available after the model has been solving:

$$y = X\hat{b} + Z\hat{p} + Z\hat{a} + \hat{e},$$

where **y** contains the observations,  $\hat{b}$  the estimates for the fixed effect factors,  $\hat{p}$  the estimates for the non-genetic animal effect factors,  $\hat{a}$  the estimates for the additive genetic animal factors and  $\hat{e}$  the residuals.

**Selected Model Factors' Sum.** Any factor included in  $\hat{b}$ ,  $\hat{p}$ , or  $\hat{a}$  can be included into the sum. All factors included into the sum have to be specified with ones (**1**); all factors excluded have to be set to zero (**0**).

**Yield Deviations** ( $YD = y - X\hat{b} - Z\hat{p}$ ). All factors associated with  $\hat{b}$  and  $\hat{p}$  have to be set to zero (**0**); all factors associated with  $\hat{a}$  have

to be specified with ones (1).

**Individual Daughter Deviations (IDD)** and **Daughter Yield Deviations (DYD)**. The **IDD** is a quantity which is need also for the calculation of the **DYD**. Thus, for both options the same quantity is needed ( $IDD = y - X\hat{b} - Z\hat{p} - 1/2\hat{a}_{dam}$ ). All factors associated with  $\hat{b}$  and  $\hat{p}$  have to be set to zero (0); all factors associated with  $\hat{a}$  have to be specified with ones (1).

**VAROPT** A line with one entry that specifies different options related to the adjustment for heterogeneous variance or to the [estimation of variance components](#).

**n None.** None of the options are requested.

**e <f n> Estimation of Variance Components.** The option **e** will instruct `mix99s` to estimate variance components by a stochastic Monte Carlo Expectation Maximization REML (**MC EM REML**) algorithm (for more information please see chapter 9). An additional (optional) instruction can be given after the **e** character. This instruction has two entries; the character **f** and an integer number *n*. The optional instructions are needed in case certain variance component parameters are meant to be [fixed](#). This option will be explained in chapter 9. For common analysis, where only an **e** is defined on the **VAROPT** option line, three additional instruction lines have to be given.

**STOPE** The first line contains three entries, two integers followed by one real value. The first integer value specifies the maximum number of **MC EM REML** rounds. The second integer value specifies the [number of data samples](#) generated and analyzed within a **REML** round. The real value is the stopping criterion for the **REML** analysis. After the [convergence indicator](#) reaches a value smaller than the specified convergence criterion, the **REML** analysis will perform a sequence of final 30 **MC EM REML** rounds, which will eliminate the Monte Carlo error from the parameter estimates.

**Default values: 1000 5 1.0e-9**

**SEED** The second line contains one entry, which defines the type of the seed used by the random number generator for generating the data samples.

**d** Default initialization by call to `random_seed`.

**r** The random number generator is initialized base on the system clock.

**g** The user can specify the seeds for the random number generator. If option **g** is specified *j* integers must be provided.

**Default value: d**

**MIX99PATH** The third line contains the path for the directory where the `mix99i` pre-processor executable is located. In certain intervals the `mix99s` solver will make a system call to `mix99i` to update the preconditioner matrices as explained in chapter 9. This will also cause an update of the `MiX99.lst` file. Variance components listed are not anymore the starting values used, but the intermediate estimates that were applied for the most recent preconditioner matrix update. If the given directory name is empty (either a pair of quotation marks ("") or minus sign (-)) the pre-processor is assumed to be located in a directory that is included in the search PATH.

- s** **Start-up cycle for heterogeneous variance adjustment.** After `mix99p` has performed a maximum number of 20 iterations (specified on the `STOP` option line) it will write heterogeneity of variance estimates to files named `SiWi.data(i)`. These files will be used by `mix99hv` to create the input data files for the applied variance model that describes the heterogeneity of variance in the data.
- c** **Cycle between models for solving the multiplicative mixed model.** The option is needed for the heterogeneous variance adjustment and will instruct `mix99p` to discontinue in certain intervals the iteration process and make system calls for solving the variance model by a second, simultaneous **MiX99** analysis. The process will continue until both models have converged.

**ADJUST** In case **s** or **c** is defined on the `VAROPT` option line, an additional line needs to be specified with as many integers as there are factor columns defined in the `REGRESS` instruction line. This is equal to the first integer value of the `REGRESS` instruction line (see *Technical reference guide for MiX99 pre-processor*). The order of the integer values on the `ADJUST` line corresponds to the order of the factors specified on the `REGRESS` instruction line. Each integer specifies whether or not the corresponding factor of the model is included into the adjustment of heterogeneous variance.

- 1** The factor will be included into the HV adjustment.
- 0** The factor will be excluded from the HV adjustment.

Including all factors corresponds to the method by Meuwissen et al. (1996). When excluding some factors from the HV adjustment a restricted multiplicative mixed model will be applied. Excluding the fixed effect factors from the example model given in `VALID` will perform a restricted multiplicative mixed model adjustment for heterogeneous variance of the form:

$$y_i = X_i \hat{b} + (Z_i \hat{p} + Z_i \hat{a} + \hat{e}_i) \gamma_i,$$

where  $\gamma_i = \frac{1}{\lambda_i}$  and  $\lambda_i$  is the heterogeneous variance adjustment factor for stratum  $i$ .

**STOPC** In case **c** is defined on the **VAROPT** option line, a second additional line with two entries must be given. The first entry is an integer value giving the maximum number of **heterogeneous variance adjustment** cycles; i.e. the maximal number that the **variance model** will be updated and solved. The second entry is a real value and is the required stopping criterion. The updating and solving of the **variance model** will stop when the **convergence indicator** for the heterogeneity adjustment factors has reached a value smaller than the specified stopping criterion. The **convergence indicator** for the heterogeneity adjustment factors is calculated as:

$$cd_{(k)} = \frac{(\mathbf{l}^{(k)} - \mathbf{l}^{(k-1)})^T (\mathbf{l}^{(k)} - \mathbf{l}^{(k-1)})}{(\mathbf{l}^{(k)})^T (\mathbf{l}^{(k)})},$$

where  $cd_{(k)}$  is the value of the convergence indicator in adjustment cycle  $k$  and  $\mathbf{l}$  is the vector of multiplicative adjustment factors (lambda values).

**Default values: 80 1.0e-7**

**SOLTYP**

A line with one character, which specifies the way solutions are handled. This option became necessary when modules for solving different non-linear models were implemented in the **MiX99** package. For solving standard linear models a **y** must be specified. All other options are related to **adjustment of heterogeneous variance** or to **non-linear Gompertz models**.

- y** **Yes, give standard solution files.** Solution files are written in text format.
- n** **No.** No solutions are written. This is useful when specifying option **s** on the **VAROPT** option line.
- d** **DMUINPformat.** Option will produce binary and ascii files with the pseudodata. See 8.2.2. This option is needed only for a simultaneous estimation of variance components for the non-linear Gompertz function model by, for example, using the DMU package for the variance component estimation.

One of the two options (**a**, **h**) must be defined when using **MiX99** for solving the **variance model** for **adjustment of heterogeneous variance**. The option will instruct **mix99p** to accelerate the solutions of the **variance model** between consecutive **heterogeneous variance adjustment** cycles. The solutions are written to binary files (**SolfixB** for strata of the first effect and **SolaniB** for strata of the second effect in the **variance model**).

- a** Accelerated solutions using Aitken acceleration. This option is suitable, if convergence is dominated by a single large eigenvalue. For many models it yields fast convergence (between 40 to 60 cycles).
- h** Accelerated solutions using a Half-Chebyshev golden ratio procedure (**Hesterberg, 2005**). This step-lengthening method follows a golden ratio procedure. For large and complex models it was found

more reliable but it requires between 80 to 100 cycles. The option is robust and therefore recommend for routine evaluations.

## 4.2 Determining convergence

The solver programs `mix99s` and `mix99p` provide four different **convergence indicators**. The convergence indicators are calculated after each round of iteration and are written to the standard output. The first three convergence indicators are norms and for describing these norms we define that  $C$  represents the coefficient matrix of MME,  $\hat{\mathbf{s}}^{(k)}$  the vector of solutions at round  $k$ ,  $\mathbf{r}$  the right hand side of the MME, and  $M^{-1}$  the inverse of the **preconditioner** matrix, which approximates the inverse of  $C$ . The three norms are:

$$\begin{aligned}
 ca_{(k)} &= \sqrt{\frac{(\mathbf{r} - C\hat{\mathbf{a}}^{(k)})^T (\mathbf{r} - C\hat{\mathbf{a}}^{(k)})}{(\mathbf{r}_a)^T (\mathbf{r}_a)}}, \\
 cr_{(k)} &= \sqrt{\frac{(\mathbf{r} - C\hat{\mathbf{s}}^{(k)})^T (\mathbf{r} - C\hat{\mathbf{s}}^{(k)})}{(\mathbf{r})^T (\mathbf{r})}}, \\
 cd_{(k)} &= \sqrt{\frac{(\hat{\mathbf{s}}^{(k)} - \hat{\mathbf{s}}^{(k-1)})^T (\hat{\mathbf{s}}^{(k)} - \hat{\mathbf{s}}^{(k-1)})}{(\hat{\mathbf{s}}^{(k)})^T (\hat{\mathbf{s}}^{(k)})}},
 \end{aligned}$$

where  $ca_{(k)}$  is the relative differences between left-hand side and right-hand side of the part of the MME which includes the equations of the additive genetic animal effects;  $cr_{(k)}$  is the relative differences between left-hand side and right-hand side of the MME; and  $cd_{(k)}$  is the relative differences between solutions of consecutive iteration rounds.

The norms  $ca_{(k)}$  and  $cr_{(k)}$  are the most reliable convergence indicators. Convergence behaviour when solving a model, where these both norms are getting smaller each round of iteration indicates that estimates are converging towards the true solutions of the MME. By definition of the conjugate gradient methods, every additional conjugate gradient step will move the estimates closer to the true solutions of the MME and thus both norms are getting smaller. However, for some models especially  $cr_{(k)}$  can show an erratic behaviour. This is because  $M^{-1}$  is not included into the calculation of the norm. Moreover, the size of the norm varies between models. Because of the latter two characteristics it is necessary to find for each model the appropriate stopping criterion in case the stopping criterion is applied to norm  $ca_{(k)}$  or norm  $cr_{(k)}$ .

The norm  $cd_{(k)}$  is widely used because it's easy to calculate and has very smooth convergence behaviour. The norm is almost independent from the applied model and it has been found that a value smaller than  $1 \times 10^{-4}$  indicates sufficient convergence for the vast majority of models solved by **MiX99**. However, a disadvantage of the norm is that a small value of the norm is no guaranty that real convergence has been achieved.

The fourth convergence indicator gives the largest change of an estimate between the last two iterations out of all estimates. A large value at the end of the iteration process usually indicates that some fixed effect classes have very few observations and no unique estimate is found for some effect levels. For many models it has been found that this indicator should converge to a value smaller than  $1 \times 10^{-1}$ .

In case of solving the [multiplicative mixed model](#) for the [heterogeneous variance adjustment](#) (option **c** at the **VAROPT** line) only one convergence indicator is provide during the HV cycling process. For computational ease this criteria is:

$$cm_{(k)} = \sqrt{\frac{(\mathbf{r} - \mathbf{C}\hat{\mathbf{s}}^{(k)})^T (\mathbf{r} - \mathbf{C}\hat{\mathbf{s}}^{(k)})}{(\mathbf{r})^T \mathbf{M}^{-1} (\mathbf{r})}},$$

which is otherwise the same as  $cr_{(k)}$  but including the  $\mathbf{M}^{-1}$  matrix in the calculation.

#### 4.2.1 Choosing a suitable convergence criteria

Each of the three available norms for indicating progress of convergence has its own characteristics as described above. Based on the experiences which we and the **MiX99** users gained by solving very different models of very different size, we recommend the following alternatives ways to secure sufficiently accurate converged solutions:

**Alternative 1:** Apply a convergence criterion of  $1 \times 10^{-4}$  (or between  $1 \times 10^{-4}$  and  $1 \times 10^{-5}$ ) to the convergence indicated **CD** and check that the convergence indicators **CA** and **CR** show progress of convergence during the whole iteration process.

**Alternative 2:** Apply the convergence criterion to the convergence indicator **CA** and define a convergence criterion, which will ensure that the convergence criterion **CD** will have reached a value smaller than  $1 \times 10^{-4}$  at the end of the iteration process.

For some **large routine evaluations** solving time might be critical, and the solver should carry out only the least number of required iteration rounds to achieve sufficient convergence of the solutions. For such evaluations the most suitable convergence criterion is found by comparing solutions of several test runs, where different strict convergence criteria were applied, with “quasi-true” solutions from a test run with a very strict convergence criterion (e.g.  $cd_{(k)}$  norm between  $1 \times 10^{-5}$  and  $1 \times 10^{-6}$ ). For many models it was found that a correlation of  $\geq 0.995$  of the genetic animal effect solutions with the “quasi-true” genetic animal effect solutions indicate that sufficient convergence has been achieved ([Lidauer and Strandén, 1999](#)).

#### 4.2.2 Effect of preconditioning on convergence

The choice of [preconditioner](#) matrices can have significant effect on speed of convergence when solving complex models. Generally, the better the inverse of the preconditioner matrix approximates the inverse of the coefficient matrix of the MME, the faster convergence of the solutions is achieved. However, specifying large preconditioner matrices may cause a considerable increase in computations at the cost of total solving time.

The following example demonstrates that the specified [preconditioning](#) can significantly affect the solving time. For specifying the preconditioner matrices, please see **PRECON** instruction line in the [Technical reference guide for MiX99 pre-processor](#).

The **example** data included 374007 test-day records from 19709 cows of 130 herds. The data was modeled with a multiple trait random regression model including nine traits. The model including four fixed effects, a random herd-test-day effect and functions for the within-herd lactation curve, the non-genetic animal effect, and the additive

genetic animal effect. To make the solving of the model as demanding as possible, no rank reduction was applied. This yielded (co)variance matrices of size 9, 27, 36, 36, and 9 (for the residual), respectively. The MME included over 2 million equations.

Here, the effect of three different [preconditioning](#) alternatives will be demonstrated: Alt.1) a diagonal preconditioner for all effects; this is equal to the diagonal of  $C$ . Alt.2) a block diagonal preconditioner for all effects; the block size varied between 9 and 36 depending on the effects. Alt.3) a block diagonal preconditioner for all random effects and one full block preconditioner matrix including all fixed effect equations, which was of size  $7401 \times 7401$ .

Solving was continued until the [convergence indicator](#)  $cd_{(k)}$  was smaller than  $3.16 \times 10^{-5}$ .

Preconditioner alternative	Number of Iterations	Solving Time (min)	Size of Preconditioner (Mb)
Alt 1) Diagonals	3725	56.3	8
Alt 2) Block diagonal	584	13.6	140
Alt 3) Block diagonal + full block	598	24.0	25

Applying a [block diagonal preconditioner](#) matrix for all effects yielded the shortest solving time, whereas apply a [diagonal preconditioner](#) matrix for all effects yielded the smallest preconditioner matrix. Experiences showed that a [block diagonal preconditioner](#) is a good choice for many different models. For very large models the size of the preconditioner matrices might be critical. Then, a diagonal preconditioner needs to be applied for some of the effects in the model.

### 4.3 External STOP

In some situations it might be useful that the iteration process is stopped in a controlled fashion before one of the specified stopping criterions has been fulfilled. The solver programs can be instructed to stop after the current round of iteration by creating a file named `STOP` in the directory where the solver is executed. Then, the solver will write the most recent solutions to the standard solution files. When [parallel computing](#) is applied, the `STOP` file has to be accessible by the master process. In case [heterogeneous variance](#) is accounted, a `STOP` file can be used to stop the cycling between [mean model](#) and [variance model](#). Then, after the current adjustment cycle is finished, the program will continue with iterations on the [mean model](#) until a stopping criterion is reached or the `STOP` file is provided a second time. The solvers will erase the `STOP` file from the directory to avoid trouble in future analysis.

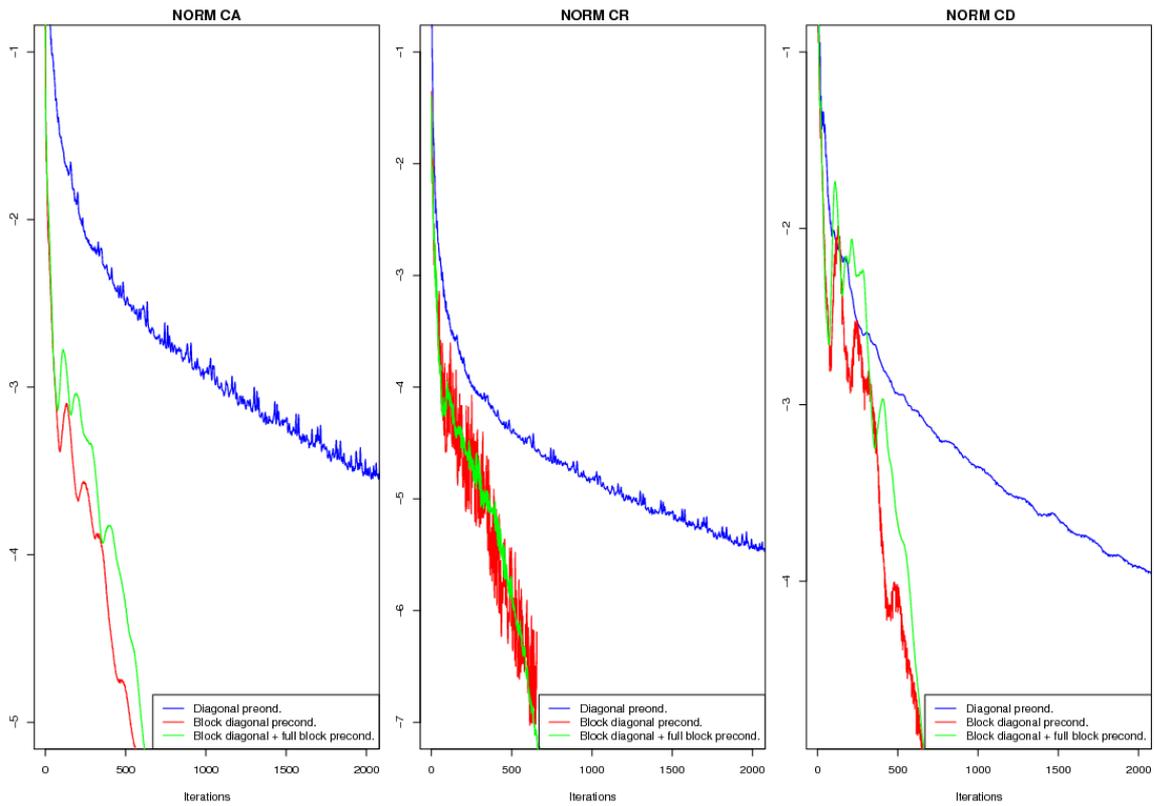


Figure 1: Logarithm of the convergence indicators norm CA, norm CR, and norm CD by round of iteration, given for different preconditioning alternatives when solving a complex model.

## 5 Output files of the MiX99 solvers

### 5.1 Standard output

The solver programs `mix99s` and `mix99p` will write information about the specified solver options, about the iteration process as well as a sample of solutions and the description of the solution files to standard output.

### 5.2 Solution files

#### 5.2.1 Formatted solution files

The structure of the standard solution files depends on the model. Therefore, the solvers write for each solution file an explanation to the standard output after the solving procedure has finished.

- Solani** Solutions for additive genetic animal effects.
- Solfix** Solutions for all across blocks fixed effects.
- Solfnn** Solutions for the  $n^{\text{th}}$  within blocks fixed effect. E.g., `SolF02` is the solution file for the 2<sup>nd</sup> within block fixed effect.
- Solrnn** Solutions for the  $n^{\text{th}}$  random effect in the model. E.g., `Solr03` is the solution file for the random effects with the random effect number 3. Solution files for the random effects are optional (see `RANSOLFILE` instruction line in *Technical reference guide for MiX99 pre-processor*).
- Solreg** Solutions for the regression effects applied across the whole data. (Specified on the `REGRESS` instruction line. see *Technical reference guide for MiX99 pre-processor*).
- Soldyd** Solution files with [daughter yield deviation](#) for sires.
- Sol\_mn** For some `LS-models` only. Solution file with the estimate for the mean.

#### 5.2.2 Unformatted solution files

The *MiX99* solvers write solutions to unformatted files which will allow a restart of the solvers with the solutions given in these files.

- Solvec** The `mix99s` solver writes a copy of the solution vector to this file after the end of the iteration process. At each start of `mix99s` the program will check whether a `Solvec` file is provided, and if so, it will initialize the solution vector with solutions given in `Solvec`. Thus `mix99s` can be restarted without running the pre-processor.

Note, the pre-processor `mix99i` will erase an old `Solvec` file. In case the `mix99i` pre-processor is instructed to include old solutions, it will create a `Solvec`, which will be read by the solver. For instructing MiX99 to read old solutions please see `SOLUNF` instruction line in the *Technical reference guide for MiX99 pre-processor*.

- Solpriv(i)**, **Solcommon** These files contain the solutions private to each process and common to each process. These files allow restart of the `mix99p`

solver. The files have the same meaning as the `Solvec` file for the `mix99s` solver.

**Solunf** Contains all solutions to the MME and the original ids of all effect levels. This file is optional (see `SOLUNF` instruction line in the *Technical reference guide for MiX99 pre-processor*) and can be rather large. The file can be used to initialize, in a future evaluation when more data has accumulated, the solution vector with old solutions. For a future evaluation the file must be renamed to `Solold` to be read by the `mix99i` pre-processor.

### 5.3 Files for model validation purposes

The solver programs can be instructed to provide information useful for model validation purposes or information need for other type of analyses. The specified option on the `RESID` and `VALID` option lines will instruct which of the following unformatted files are created:

- eHat.data (i)** File(s) with [residuals](#).
- yHat.data (i)** File(s) with [predicted observations](#).
- sHat.data (i)** File(s) with a [sum of selected model factors](#).
- YD.data (i)** File(s) with [yield deviations](#).
- IDD.data (i)** File(s) with [individual daughter deviations](#).

The `mix99s` solver will create one file only with a zero character (0) added at the end of the file name. The `parallel` solver `mix99p` will create as many files as there are processes specified for the parallel run. The files are numbered by (i), where (i) goes from zero to number of processes minus one and the number is added at the end of the file name.

The file(s) contain strictly as many rows as there are data rows in the input data file, regardless whether some input data is missing or not used in an analysis. The order of the rows is consistent with the order of the data rows in the input data file. Each row consists of a fixed number of real values, which depends on the applied model. The number of real values is the same on all rows and is equal to the number of traits in the largest trait group. This number is equal to the `mxntra` parameter in the `Parlog` file. The `Parlog` file is produced by `mix99i` pre-processor. The real values in a particular row correspond to the trait group that is specified on the corresponding data row in the input data file. The order of the values within a row corresponds to the order of the traits within a trait group as specified on the `MODEL` instruction lines (see *Technical reference guide for MiX99 pre-processor*). In case an observation is missing in the data file or it is not used in the analysis, a [missing value](#) variable will be written for the corresponding real value. This [missing value](#) variable is `-8192.0`. In case the `SCALE` option is used, all information will be transformed back to the original scale before writing to the files.

All values on a row are stored as single precision real values and simple Fortran programs can be written to transfer the files to text files. However, the **MiX99** packages provides `MiXtools` programs, which allows simple analyses of the information (means and SD by classification), or merging of the files with the input data file. See

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

`MiXtoolmerge.f90` and `MiXtoolms.f90` in the `MiXtools` directory of the package.

## 6 Reliabilities

### 6.1 Approximate reliabilities using ApaX

Sometimes reliabilities or accuracies of estimated breeding values are needed, e.g., Interbull requires reliabilities for the evaluated bulls. Reliabilities need elements of inverse of the mixed model equations (MME). Exact inverse of MME cannot be computed in most cases due to computing time or memory limitations. Thus, approximations need to be used. A separate program named `apax99` has been made to calculate approximations to reliabilities. A [parallel computing](#) version has been written as well, named `apax99p`.

In general, ApaX was made to handle linear animal models. However, even here there are restrictions. Some new features are not supported. For example, no additional correlation files (needed by MAS BLUP), or regression design matrices (needed by genomic BLUP) are accounted by ApaX.

Four approximation methods to calculate reliabilities have been implemented with some additional ones being variations of these four methods. The approximation methods have two steps ([Strandén et al., 2000](#)). The first step accounts for data design, and the second step accounts for relationship information. The first step is the same for all approximation methods and is computationally most demanding. This step uses [parallel computing](#) in `apax99p`.

The following calculation methods are base to all available methods:

- 1) Interbull reliabilities ([Strandén et al., 2000](#))
- 2) Misztal and Wiggans approach ([Misztal and Wiggans, 1988](#))
- 3) Jamrozik et al. approach ([Jamrozik et al., 2000](#))
- 4) Tier and Meyer approach ([Tier and Meyer, 2004](#))

Reliabilities by method 4, i.e., Tier and Meyer approach, are available only in the single processor version `apax99`.

Some notes on the base methods:

- Method 1. Calculations are based loosely on the guidelines set by Interbull, and have been accepted by Interbull to be used in the Finnish dairy cattle evaluations. There is a post-processing program called `BR2.f90` that produces the information required by Interbull from the output given by `apax99` or `apax99p`.
- Method 2. Approximation has two steps. The first step calculates information amount due to observations by model design. The second step uses the method of [Misztal and Wiggans \(1988\)](#) to incorporate relationship information.
- Method 3. Similar to method 2, except that the method by [Jamrozik et al. \(2000\)](#) is used in the second step to account for relationship information.
- Method 4. The first step is the same as in the other approximation methods 1-3. However, all subsequent calculations use matrices unlike the other approximations that rely on scalar computations for multiple trait cases as well. Because of matrix computations, method 4 often uses more mem-

ory than the other approximation methods, especially when many traits and/or random regression test day models are analyzed.

### 6.1.1 Differences of reliability calculation and breeding value estimation

In general, reliability calculation by the **MiX99** package is similar to solving MME by `mix99s/mix99p`. The `apax99` and `apax99p` programs accept data prepared by `mix99i`. There are, however, some restrictions and modifications to the regular directive files:

- 1) Only effects that are defined to be within block are considered when approximate reliabilities are calculated.
- 2) Animal genetic effects need to be the first effect in the within block equations.
- 3) No **heterogeneous variance** modeling is accounted (**multiple residual variance matrices** are, however, used in the first step when calculating cow reliabilities but not in the second step where the residual is taken from the standard variance component file).
- 4) **Preconditioner** matrix information is ignored. Thus, computationally lightest preconditioner, i.e., no preconditioner, is best.
- 5) Phantom parent groups can exist in the data and model but are not accounted in the reliability calculations. Hence, results are the same with or without phantom parent groups.
- 6) Extra correlation matrices for random effects are not accounted except in single-step model parts of the additional matrix needed by single-step are used.
- 7) Regression coefficient matrices are not accounted.

In practice, the first restriction relates to memory use. Although it is possible to have large herd blocks in breeding value estimation without problems (especially in single processor case), here such large blocks may use too much memory. It is advisable to have blocks with contemporaries in the same block as herd. If there are many animals that have observations in several blocks (e.g., herd changing cows), memory may become a limiting factor.

After running the preprocessor program `mix99i`, a program called `imake4apax` needs to be executed before running the **parallel** version `apax99p`. When breeding values are estimated, number of common blocks need to be defined. Here it does not matter how many common blocks have been given because `imake4apax` will reset this to zero.

### 6.1.2 ApaX instruction file

The **ApaX** reliability approximation programs `apax99` and `apax99p` require information, which is read by the standard input of the programs.

**Example of ApaX instruction file:**

```

1 # Reliability method (AccurType):
2 2
3 # Number of non-zeros in sparse matrix (MaxNonZ):
4 10000
5 # Original dir file (OriginalDir):
6 MiX99_DIR.DIR
7 # Absorption level effect (JFilter):
8 2

```

The information is given on instruction lines in the same order as presented below. Information that is model dependent is given in *italics*:

**AccurType** Number of approximation method:

- 1 Interbull
- 2 Misztal & Wiggans
- 3 Jamrozik et al. approach
- 4 Interbull Tier and Meyer approach (available only in `apax99`)
- 20 [Reversed reliability approximation](#)

For [parallel computing](#) there is option **1d** for the Interbull method that is for distributed memory computers. In **1d** the second step of the Interbull method uses [parallel computing](#) as well. The main advantage is distribution of memory where each parallel job uses less memory than a single processor version but combined memory use is greater.

Several additional options can be given on this line:

- O** Write `PEV.bin` file after the 1<sup>st</sup> approximation step.
- I** Read `PEV.bin`. Thus, no need to perform the 1<sup>st</sup> step.
- M** Maternal trait assumption in calculation of phenotypic variance. Thus, when additive genetics has both direct and maternal effects, it is necessary to inform the program that correct formula is used in calculation of phenotypic variance:

$$var(g_{direct}) + var(g_{maternal}) + cov(g_{direct}, g_{maternal}) + var(residual).$$

- R** Maternal genetic reliabilities. This option informs that maternal trait reliabilities should be calculated instead of direct genetic reliabilities. Please use option **M** as well to have phenotypic variance calculated properly.
- L** Long output listing. Default is short output listing.
- P** Pedigree file name given instead of original directive file name (for [reversed reliability approximation](#)).

Options **O** and **I** allow quicker execution when multiple approximation methods need to be executed. For example, method 1 and 2 reliabilities need to be calculated. First, make method 1 reliabilities and write file `PEV.bin`. Then, `PEV.bin` is read (input) and used in a subsequent run to calculate method 2 reliabilities without the time consuming 1<sup>st</sup> step. Note that the directive files (for `mix99i` and `apax99`) need to be exactly the same in the two runs except for change in first command line to

apax99 where reliability calculation method and options can be changed.

**MaxNonZ** Maximum number of non-zeros in the sparse matrix of the largest block. The program will process data block by block, and build coefficient matrix of the mixed model equations (MME) for the equations within block. MME of each block is stored as a sparse matrix, and, here, maximum number of non-zeros element in the sparse matrix is given.

It is not necessary to know exactly this value because dynamic memory allocation approach is used to increase size of the sparse matrix. However, it may be good to have a reasonable value for the required size. The implemented dynamic memory allocation approach increases sparse matrix by 50% when the matrix becomes full. Consequently, memory may be reserved more than actually required (at most 50% more).

In shared memory [parallel computers](#) this may be very important. Note that if memory is increased above available memory, less than 50% is added. Eventually, no memory can be added to increase sparse matrix size, and then disk is used through file `Sparse_Matrix.DMPz` where z is the process number. Note that this will slow computations considerably. Naturally, the sparse matrix cannot grow beyond size of available disk memory.

**StartDIM** **OPTIONAL: asked only when a [covariable table](#) was given in the directive file.** Starting index value of the first line in the [covariable table](#), if [covariable file](#) is present. The data file has index values (see 7.3) that correspond to lines in the covariable file. Each line of the covariable line is stored internally in **MiX99** compactly such that the starting index value is lost. This information has to be given again here. In dairy cattle, this is often the lowest value for days in milk.

**CovarInfo** **OPTIONAL: asked only when a [covariable table](#) was given in the directive file.** One line for each model line in the directive file for `mix99i`, if [covariable file](#) is present. Each line has 3 numbers: Smallest [covariable table](#) index value used for the breeding value index using random regressions, number of [covariable table](#) calculation points, and distance between the points. For example, if breeding value is defined by calculating random regressions from days in milk every day from 8 to 312 (to get 305 day breeding values), then a triplet 8 305 1 is given (StartDIM above must be 8 or lower). If the days are from day 15 every 30<sup>th</sup> day for 10 points, then the triplet is 15 10 30.

**OriginalDir** Name of the original directive file given to the pre-processor program `mix99i`.

**NumBVs** **OPTIONAL: Asked only when there are more than one trait in the model.** Number of breeding values to be calculated. Zero (0) indicates breeding values for all traits with default [Weights](#). Zero is allowed only for models for which the default weights can be deduced. NOTE: the value can be at most number of traits.

- Weights** ***OPTIONAL: Asked only when [NumBVs](#) is greater than 1.*** A line for each breeding value index ([NumBVs](#)). Each line gives weights according to the breeding value index wanted. Number of weight values on each line is equal to the number of traits in the model. For example, there are three traits in the model. Now, an index weight line has three values, each informing how the traits are weighted in a breeding value index. A valid line would be like '1 1 0' where the first two traits are weighted equally but last one is not accounted.
- H2calc** ***OPTIONAL: Asked only when there are more than 2 random effects, i.e., more than just genetic and residual random effects.*** Random effect numbers included in the calculation of phenotypic variance in heritability, if more than 2 random effects (i.e. additive genetics and residual) in the model. The two last random effects (genetic and residual) are automatically included in the calculation of phenotypic variance of heritability. However, when there are other random effects as well, their inclusion is asked here. The random effects are numbered as in the parameter file for variance components. For example, there are five random effects: herd test month (number 1), first permanent environment (2), second permanent environment (3), additive genetic (4), and residual (5). If all but herd test day is wanted in the heritability then a line '2 3' is given indicating that second and third random effect are included in the phenotypic variance.
- JFilter** Calculation of reliabilities is programmed such that all within block effects are absorbed to the animal genetic effects. They can be absorbed either exactly or approximately. JFilter describes which effects are approximately absorbed. If the exact absorption is done, the sparse matrix may be filled and exhaust available memory. In addition, the computations may be slow. Therefore, some effects can be only approximately absorbed with no additional fill-in to the sparse matrix. In order to minimize memory use in absorption, ordering of the effects within block should be such that the smallest number is given to an effect with observations from a single animal and larger numbers to the effects with observations from several animals. Effects are ordered as given in the [within block ordering](#). Exact absorption is commonly done for the effects that are within animals such as permanent environmental effects. For example, let's consider a case in which we have three within block effects: 1) genetic, 2) permanent environment, and 3) herd year. If we want to absorb the herd effect approximately, the JFilter value of 3 is given. Thus, only the permanent environment effect (effect 2) is exactly absorbed to the genetic effects. In a situation, in which we want to exactly absorb all other within block effects to the genetic effects (n within block effects), a value of n+1 should be given to the JFilter. In the example given above, JFilter would be 4.

### 6.1.3 Guidelines for determining blocking and JFilter

Two of the most difficult variables affecting reliability calculations are blocking ([SORT\\_R](#)) and absorption level ([JFilter](#)). Some guidelines for reliability calculations:

- 1) Start model building for reliability calculations from a simple to a more complex

model.

The simplest model for reliability calculations should have the genetic effects and non-genetic animal effects (e.g., permanent environment). Then, some kind of management effect can be tested in the model. Management effects are commonly approximately absorbed (see next comment) and can create problems in absorption process. Look at the output. Perhaps, there are many management effects or alternatives. Test them separately. The less there are messages of type 'ABSORB: Singularity in row' the better from numerical calculation point of view.

2) Have only one effect per trait absorbed approximately.

When several effects are absorbed approximately, they tend to double count information, and may lead to negative information which is seen as messages of singularity given by the absorption procedure. Approximate absorption does not account possible co-linearity or other correlations in design between effects. As an extreme case, assume an effect being twice in the model and both effects are absorbed approximately. Then, the other effect will lead to double accounting of the effect, because approximate absorption does not notice that the same effect is twice in the model. This means that prediction error variance left for an individual can become negative. In general, this is the more likely the less there are number of observations in an effect class, e.g., small herd and herd-year classes.

The approximately absorbed effect from the full model should be the one with most levels for the model to account best management effect from modelling point of view. This effect is typically a herd management effect by time effect like herd-year. Unfortunately, this can be numerically the worst effect. Sometimes it is possible to have more than one effect per trait if all approximately absorbed effects are random. However, this is very rare due to likely increase in numerical problems.

3) All effects close to animal (e.g., permanent environment) should be absorbed exactly. These effects do not result in additional fill-in, if order of observations for an animal can be such that they are close to each other. If observations of an animal are in different blocks, then memory is used more.

4) Blocking should be used to group animals by the herd management effect in the model (management without time) for efficient memory management.

- If there are too many blocks, then memory is used too much because many animals tend to become block/herd changers.
- If there are not enough blocks, memory is again used too much, because all information for a block is read to memory.

5) If there is a maternal effect in the model, try to have dam in the same block as its offspring with observations. When dam is in a different block than any of its offspring, the two blocks are connected, and there are block changer equations. **ApaX** will make a separate block from these block changers. The block should be kept as small as possible for memory reasons by ordering as many dams as possible to the same blocks as their offspring with observations.

If there are problems with reliability calculations, it is best to start with a simple model which has only animal genetic effect. Then increase level of complexity in the model. Problems in reliability calculations involve: long computing time, unusual reliabilities

(close to one without reason), diminishing reliability with increased data. Changes in blocking strategy, absorption level or effects in the reliability calculations model are most likely to cure any problems.

Finally, one useful strategy in understanding reliability calculations is to have a dummy pedigree where all animals have unknown parents. Reliabilities using such pedigree can be compared with reliabilities by complete pedigree information (using methods 2 and 3). Comparison shows if the problems are due to pedigree, and not due to above mentioned variables. In addition, it gives information on which animals are the ones with most problems.

#### 6.1.4 ApaX Output files

Once `apax99` or `apax99p` has been executed, the reliabilities will be written to a solution file, called `PEVani`. The solution file has similar structure to the solution file `Solani` produced by the solver programs. However, the `PEVani` file has a different format depending on the computing method used. When the Interbull method is used each line has both effective daughter contributions (EDC) and reliabilities. When any other method is used then only reliabilities are given, and the format of the file is exactly the same as `Solani`.

The `PEVani` file produced by the Interbull method can be made more accessible by program `BR2.f90`. This program expects that files `PEVani` and `BR2.dat` written by `apax99/apax99p` are available. In addition, names of two files are asked:

**SireFile** This file has id numbers of all the sires for which the sire reliabilities were calculated. The file should be a regular text file with each line having a bull id number as the first number.

**OutFile** This is the output file that will be generated.

Each line of the output file has the following information:

- 1) Id number of a bull.
- 2) Effective daughter contributions (EDC) for each breeding value requested.
- 3) Reliability for each sire breeding value requested.

#### 6.1.5 Example of ApaX instruction file

##### **ApaX99 instruction file:**

```

1 # Type of analysis: 1= Interbull accuracies
2 1
3 # Maximum number of non-zeros in the sparse matrix
4 600000
5 # Start DIM in covariable table file,
6 1
7 # For each model line: First DIM, Number of DIMS, DIM step
8 8 305 1
9 8 305 1
10 8 305 1
11 # Original directive file given to mix99i
12 miniT.mix
13 # Number of breeding values
14 3
15 # Weights for breeding values

```

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

```

16 1 0 0
17 0 1 0
18 0 0 1
19 # random effects accounted in h2 calculations
20 2
21 # Absorption level effect
22 3

```

### **MiX99 instruction file for mix99i (miniT.mix):**

```

1 # Estimation of breeding values for milk, protein kg and fat kg for the
2 # Finnish dairy cattle using a multiple trait random regression test day
3 # model based on covariance functions. Reduced data and model: only first
4 # lactation included.
5 # -----
6 # title
7   Finnish RRTD-Model; first 0.1% of data from 1988 to Feb. 2000
8 #INTEGER
9   herd animal trgrp cowxlac hy htd mg ym yr_sea age dcc dim
10 #REAL
11   milk protein fat
12 # traits
13   3
14 # trait-groups, input column
15   1 3
16 # input column of block code and relationship code
17   1 2
18 # number of fixed- and random factors columns in the model lines
19   8 13
20 # MODEL:
21 # | fixed effects |ran|non-hereditary | add. genet.
22 # | | season | |dom| across 1&2 L | animal eff.
23 #s t wt|s1 s2 s3 s4 s5|age dcc ym|htm|n1 n2 n3 n4 n5 n6|a1 a2 a3 a4 a5 a6
24 1 1 - 9 9 9 9 9 10 11 8 6 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
25 1 2 - 9 9 9 9 9 10 11 8 6 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
26 1 3 - 9 9 9 9 9 10 11 8 6 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
27 # order of effects within block
28 - - - - - - - - 3 2 2 2 2 2 2 1 1 1 1 1 1
29 #htm n1 n2 n3 n4 n5 n6 a1 a2 a3 a4 a5 a6
30 1 2 2 2 2 2 2 3 3 3 3 3 3
31 1 - - - - - - - - - - - - - -
32 1 - - - - - - - - - - - - - -
33 # pedigree for animal effects: num: a1 a2 a3 a4 a5 a6
34 6 1 1 1 1 1 1
35 #n s1 s2 s3 s4 s5| age dcc ym|htm|n1 n2 n3 n4 n5 n6| a1 a2 a3 a4 a5 a6
36 21 t1 t2 t3 t4 t96 cl cl cl cl t5 t6 t7 t8 t9 t10 t59 t60 t61 t62 t63 t64
37 21 t1 t2 t3 t95 t97 cl cl cl cl t11 t12 t13 t14 t15 t16 t65 t66 t67 t68 t69 t70
38 21 t1 t2 t3 t95 t98 cl cl cl cl t17 t18 t19 t20 t21 t22 t71 t72 t73 t74 t75 t76
39 # combining of traits
40 y
41 # | fixed effects |ran| non-hereditary | add. genet.
42 # | | season | |dom| across 1&2 L | animal eff.
43 # s1 s2 s3 s4 s5|age dcc ym|htm|n1 n2 n3 n4 n5 n6|a1 a2 a3 a4 a5 a6
44 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
45 2 2 2 2 2 2 2 2 2 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
46 3 3 3 3 3 3 3 3 3 3 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
47
48 # covariable file name:
49   suomiTDMpara.cov
50 # number of covariable columns
51   100
52 # integer input column in data file with covariable index (DIM)
53   12
54 # method used for relationship
55   am
56 # input file
57   Ter.dat

```

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

```
58 # int-col. real-col. form
59     12         3         f
60 # code for missing real values
61     0.0
62 # scaling (y/n)
63     n
64 # pedigree file
65     miniTDM.pedi
66 # parameter file
67     suomiTDMpara.in
68 # directory for the temporary files
69     .
70 # solution files for random effects: htm non-ac animal
71                                     n     n         y
72 # binary solution file
73     n
74 # block preconditioner WpW, XpX (=D_M)
75     d d d d
```

## 6.2 Exact reliabilities using `exa99`

Approximative reliabilities can be calculated using `apax99`. However, **MiX99** contains another program, which allows the exact calculation of accuracies via inversion of the coefficient matrix. The program is named `exa99`, has dynamic memory allocation, and is executed after running the pre-processor `mix99i`. `exa99` is only useful for small problems (up to 200 000 equations). When specifying the model in the **MODEL** line(s) of the MiX99 **instruction file** for `mix99i`, it is important to order the effects by number of levels. For within block effects, the effect with the most levels should get the lowest block ordering number and the effect with the least levels the highest. Similarly, for across block fixed effects, the effect with most levels should be specified first and the effect with the least levels should be specified last. This is important to keep the memory requirements as low as possible when inverting the coefficient matrix.

### 6.2.1 Option file for `exa99`

Execution of `exa99` requires an option file, which is read by standard input.

#### **Example of Exa instruction file:**

```
1 # Operational zero & Jarmo-filter
2 1e-5 1e-10
```

The file contains a single line with two real numbers. The first value is an operational zero (Opzero) for the diagonal elements to detect dependencies when inverting the coefficient matrix. The default value for **Opzero** is 1.0e-4. The second value is a filter (JFilter) for approximation of accuracy. If JFilter is set to a value smaller than 1.0e-10 exact accuracies are calculated. If the JFilter is set to a larger value, fill-in values smaller than the JFilter are set to zero, and hence, accuracies will be approximated. Degree of approximation depends on the chosen JFilter value.

### 6.2.2 Exa99 output files

The output files have the same setup as when solving the mixed model equations. Structure of the output files depends on the model. Therefore, explanation of the content of those files is given in the printout of the particular run of `exa99`.

- ACCani** PEV and accuracies for animal effects.
- SEfix** Standard errors for all across blocks fixed effects.
- SEfnn** Standard errors for the  $n^{\text{th}}$  within blocks fixed effect. E.g., **SEf02** is the solution file for the 2<sup>nd</sup> within block fixed effect.
- PEVrnn** Prediction error variance for the  $n^{\text{th}}$  random effect in the model. E.g., **PEVr03** is the solution file for the random effects with the random effect number 3.
- SEreg** Standard errors for the across whole data regression effects.

### 6.3 Reversed reliability approximation

The reliability calculation can be reversed so that from given reliabilities it is possible to calculate approximately **weights** that would lead back to the same reliabilities. These weights, considered as **effective record contributions** (ERC), can be derived from reliabilities, pedigree, and heritability of the considered trait using reversed Harris and Johnson algorithm ([Harris and Johnson, 1998](#)).

The reversed reliability approximation can be calculated with `apax99` (but not `apax99p`) using `AccurType 20`. The main input parameters, the reliabilities, are given to `apax99` in a separate file containing two or more columns: identification numbers and one or more reliabilities:

**File containing reliabilities for reversed reliability approximation:**

Id <sub>1</sub>	Reliability <sub>1</sub>
2	0.15809E-01
4	0.14464
5	0.14379
6	0.11543
8	0.15527
⋮	⋮

Note that the ERCs will be calculated just for those animals that are listed in the file. ERCs of other animals in the pedigree will be set to zero.

A slightly modified `ApaX instruction file` is used to calculate the ERCs from the given reliabilities. Other input information, i.e. pedigree and heritability, are either given using the original MiX99 preprocessor directive file or given directly without the need to use the MiX99 preprocessor.

- `AccurType 20` without option `p` indicates that the original preprocessor directive file name is given as `OriginalDir`:

**Example `apax99` input file of Reversed reliability approximation:**

```

1 # Reliability method (AccurType): Reversed reliability approximation
2 20
3
4 # File name of the reliability information (id and r2s):
5 id_r2s.dat
6
7 # Original MiX99 preprocessor directive file:
8 MiX99_DIR.DIR
9
10 # ERC parameters: tol  maxit  smallest [h2]
11                    1e-8  100    0.0001
    
```

whereas option `p` indicates that the pedigree file name is given instead of the original directive file name:

**Example of Reversed reliability approximation using pedigree file directly:**

```

1 # Reliability method (AccurType): Reversed reliability approximation,
2 # p = pedigree file given, no mix99i needed:
3 20 p
    
```

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

```
4
5 # File name of the reliability information (id and r2s):
6 id_r2s.dat
7
8 # Pedigree file:
9 data/AM.ped
10
11 # Number of ERC values (and r2s):
12 1
13
14 # ERC parameters: tol  maxit  smallest  [h2]
15                    0      0      0      0.33333333333333
```

In both cases the second line of the input file (**MaxNonZ**) is replaced by the name of the file containing the reliabilities.

- If **AccurType** 20 p is given, number of reliability columns in the reliability file must be given as the **NumBVs** line. This also indicates how many ERCs are calculated for each animal. **NumBVs** line must be given also for **AccurType** 20 (without option p) if there are more than one trait in the model.
- After the **NumBVs** line there must be a line containing at least three numbers for the ERC calculation specific parameters:
  - **Tolerance**: The reversed Harris and Johnson algorithm calculates the ERC values iteratively. After each step convergence of the iteration is determined by comparing the two last iterations. Convergence is achieved if the relative 2-norm of the difference is smaller than the given tolerance. Value zero indicates **default value**  $10^{-8}$ .
  - **Maximum number of iterations**: If the reversed Harris and Johnson iteration is not converged within the given maximum number of iteration, an error message is printed and the program is stopped. Value zero indicates **default value** 100.
  - **Smallest allowed ERC value**: Occasionally ERC values tend to become negative during the reversed Harris and Johnson iteration. In such cases the ERC value is replaced by the smallest allowed ERC value. Value zero indicates **default value** 0.0001.
  - **Heritabilities (optional)**: Heritability value for each **NumBVs** ERC trait or a single value for all traits. Must be given for **AccurType** 20 p but can also be used to replace the heritabilities calculated from the original preprocessor directive file (**AccurType** 20 without option p). Zero value indicates **default value** 0.5 (with option p) or value calculated from original dir file (without option p).
- **JFilter** line can be omitted.

Calculated ERC values can be obtained from the fourth column of the **PEVani** file.

## 7 Daughter Yield Deviations

The request of daughter yield deviation (DYD) for different dairy cattle studies and for [model validation](#) purposes made it necessary to implement adequate calculation procedures into MiX99. A general approach for the calculation of DYD is implemented into *MiX99*. The calculations follow the method presented in [Mrode and Swanson \(2004\)](#). For simple models, like single trait animal models, the approach will yield DYD, which are calculated in the same manner as given in [VanRaden and Wiggans \(1991\)](#). In case of random regression models, DYD coefficients will be given. These coefficients can be used in a post-processing procedure to obtain DYD for certain intervals of the time trajectory, like 305-day yield DYD.

DYDs can be obtained for each bull that has daughters with records. Furthermore, it is possible to classify within each bull the DYDs by a classification variable. This is useful for [model validation](#) purposes.

In some situations it might be useful to obtain yield deviations (YD) or individual daughter deviations (IDD). Here, an IDD is defined as the YD minus half of the dam's additive genetic animal effect. MiX99 provides an option to calculate for each observation that is included in the analysis the corresponding YD or IDD. The YDs and IDDs will be written to unformatted files. For instructing *MiX99* to calculate YDs or IDDs please see the explanations given for the [VALID](#) option in chapter 4, and about [Files for model validation purposes](#) in chapter 5.

### 7.1 Calculation of daughter yield deviations

This chapter will explain how *MiX99* can be instructed to calculate [DYD](#). Instructions have to be given for the pre-processing and for the solver programs. In case it is desired to classify the DYDs within sires, additional information will be needed in the pedigree file.

#### 7.1.1 Pedigree file

The additional information in the pedigree file is required only if [DYD](#) should be classified within sires (optional). A column with the classification variable has to be added to the pedigree file. This column must be given after the pedigree information (i.e., column 4 or higher) or after the blocking variable code in case blocking of the data is desired (i.e., in this case column 5 or higher). The classification code will indicate to which within-sire class the daughter will be grouped; e.g., the classification code could correspond with the calving years of the daughters. The classification codes need to be numbered from one (1) to n within a sire. Some classes may be missing within a sire. For animals without observations in the data file a zero (0) is given.

#### 7.1.2 MiX99 instruction file

Instructions specific to the calculation of [DYD](#) have to be given on two instruction lines. First, on the [PEDFILE](#) instruction line an integer value has to be provided after the pedigree file name. There are two alternatives available. Alternative 1: specifying a zero (0) will instruct *MiX99* to calculate DYDs for each bull with daughters that have observations. Alternative 2: Specifying the column number of the pedigree file that contains a within-sire classification will instruct *MiX99* to calculate for DYD for each

class within sire. Second, on the **PRECON** instruction line a **block diagonal preconditioner** matrix (option **b**) must be defined for the additive genetic animal effect.

### 7.1.3 MiX99 solver option file

Instruction specific to the calculation of **DYD** have to be given on two option lines. The option **d** must be specified on the **VALID** option line. This is followed by a **FACTOR** option line which specifies the model factors that are included into the DYD. Please see **Daughter Yield Deviations** in chapter 4.1, for specifying the **FACTOR** option line.

## 7.2 Solution files for daughter yield deviations

**Daughter yield deviations** are written to a file named **Soldyd**. The structure of the file is similar to that one of the file **Solani**. The structure of the file is model-specific and the solver will write an explanation to **standard output**. In case of a random regression model, **DYD** regression coefficients are given. Number and order of the coefficients is the same as for the animal effect coefficients in **Solani**. The DYD coefficients are followed by as many integers as there are coefficients for a particular DYD function. The order of these integers is the same as the order of the DYD coefficients, and the integers may have a value of one or zero. Ones indicate that the corresponding coefficients were estimable. This is important for multi-trait or random regression models, where it might be not possible that some DYD functions are not defined. For instance, given a model specifies that first and second lactation observations are different traits and all daughters of a sire have first lactation observations only. Then, there is no DYD function available for the second lactation.

For random regression models the same covariables as applied for the additive genetic animal effect apply also to the DYDs. Note: A bull's DYD function is only defined for the time interval in which the bull's daughters have observations. An extrapolation of the function beyond this time interval may yield absurd results.

## 7.3 Example

The example explained in chapter 7.3 of the *Technical reference guide for MiX99 pre-processor* will be modified for the calculation of **DYD**. Modifications are in bold.

### **MiX99 instruction file:**

```

1 # TITLE:
2   RANDOM REGRESSION, L.Schaeffer & J.Dekkers (1994)
3 # INTEGER:
4   HTD Animal
5 # REAL:
6   Covar_1 Covar_2 Milk
7 # TRAITS:
8   1
9 # TRGRP:
10  1 -
11 # DATASORT: block_code, relationship_code (single residual var.)
12  1 2
13 # FIXRAN: number of fixed and random factors in the model
14  1 3
15 # MODEL: trait_group trait weight herd-test-day gamma0 gamma1 gamma2
16           1      3      -      1      2      2      2

```

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

```

17 # WITHINBLOCKORDER: order of effects within blocks
18                               2       1       1       1
19 # RANDOM: gamma0  gamma1  gamma2
20           1         1         1
21 # RELATIONSHIPS: number: gamma0  gamma1  gamma2
22           3         1         1         1
23 # REGRESS: number  beta1  beta2  herd-test-day  gamma0  gamma1  gamma2
24           6         1         2             c1      c1      1      2
25 # COMBINE:
26           n
27 # PEDIGREE:
28           am
29 # DATAFILE:
30           example3.dat
31 # VAR:
32           2 3 f
33 # MISSVA:
34           0.0
35 # SCALE:
36           n
37 # PEDFILE: file name,          a zero for calculation of DYD
38           example3.ped              0
39 # PARFILE:
40           variance_comp.ex3
41 # TMPDIR:
42           .
43 # RANSOLFILE: animal effect
44           y
45 # SOLUNF:
46           n
47 # PRECON: block diagonal preconditioner for the animal effect in WpW
48           b       d       f
49 # PARALLEL: number of processors used by the solver program
50           1
51 # COMMONBLOCKS:
52           0

```

### MiX99 solver option file:

```

1 # RAM          RAM demand: H=high, M=medium, L=low
2               H
3 # STOP        Maximum_number_of_iterations, Stopping_criterion (CR)
4               1000      1.0e-7      r      f
5 # RESID       Calculate residuals? (Y/N)
6               N
7 # VALID       D for calculation of DYDs
8               D
9               # FACTOR: beta1 beta2 herd-test-day gamma0 gamma1 gamma2
10              0       0       0       1       1       1
11 # VAROPT     (N, S, C, E, G)
12             N
13 # SOLTYP     Type of solution files? (N,Y,A,H)
14             Y

```

### Description of the *Soldyd* file written by the solver to standard output:

```

1 .
2 .
3   Daughter Yield Deviations
4   -----
5
6   First 50 Solutions
7   -----
8       Sire   Class  N-Daug.  N-Rec.  Effect  Trait  Solution  Def.
9           9     1      2       9       1     1     -2.98764    1
10          9     1      2       9       2     1     0.488173E-01  1

```

# TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

11	9	1	2	9	3	1	0.284341	1	
12	10	1	2	9	1	1	3.74280	1	
13	10	1	2	9	2	1	-0.433969E-01	1	
14	10	1	2	9	3	1	-0.516160	1	
15	11	1	2	5	1	1	-1.03777	1	
16	11	1	2	5	2	1	0.841567E-02	1	
17	11	1	2	5	3	1	0.498087E-01	1	
18									
19	"Soldyd"-File: Daughter Yield Deviations for Sires								
20									
21	Column	Description							
22	-----								
23	1	Code of Sire							
24	2	Within Sire Classification							
25	3	Number of Daughters							
26	4	Total Number of Records							
27	5	DYD Solution / Coefficient : Factor						1 Trait	1
28	6	DYD Solution / Coefficient : Factor						2 Trait	1
29	7	DYD Solution / Coefficient : Factor						3 Trait	1
30	8	DYD is defined (yes=1,no=0): Factor						1 Trait	1
31	9	DYD is defined (yes=1,no=0): Factor						2 Trait	1
32	10	DYD is defined (yes=1,no=0): Factor						3 Trait	1
33	.								
34	.								

## 8 Non-linear models

Two non-linear models are implemented into MiX99. Estimation of categorical variables is implemented by the generalized linear mixed model with the probit link function, and estimation of the growth curve models is implemented by linearization of non-linear [Gompertz function model](#) using second order Taylor series expansion. Use of these models is still exiguous and extensions of the MiX99 program for these models are therefore considered as test-versions. There is no possibility to give the [CLIM command file](#) for these models yet. Instead, the MiX99 [instruction file](#) should be made.

### 8.1 Threshold-model

Prediction of breeding values is possible for models with one categorical and several linear traits. Models are allowed to have [missing traits](#) and unequal design matrices for traits. Thresholds can be estimated or set to be known. (Co)variance components have to be known and residual variance of the categorical trait should be set to one.

#### 8.1.1 Instruction file for `mix99i`

The categorical trait is defined by giving **T<sub>n</sub>**, where n is a number of thresholds, on its own column between first and second parameters in the [MODEL](#) line. For example, for a binary trait (recorded as 1 and 2) option **T1** needs to be marked. In case of a multiple trait model, the linear traits are defined first (see [example 7.9](#)). When the threshold model is defined, one or two additional instruction lines must be given right after the [MODEL](#) line.

First additional line defines the method that is used to analyse the threshold models. There are two options: **em** option defines the Expectation Maximization algorithm (EM) ([Gilmour and Thompson, 1998](#)) and **nr** option defines the Newton-Raphson algorithm (NR) ([Janss and Foulley, 1993](#); [Hoeschele et al., 1995](#)). By default, thresholds are estimated simultaneously. Optionally, additional characters “**ft**” can be specified to indicate fixed threshold values. Thus, a new line must follow, where the threshold values for categorical trait are defined. This line should contain as many real numbers as defined for the categorical trait in the [MODEL](#) line.

#### 8.1.2 Stopping criteria file for `mix99s`

Solving of the [threshold-model](#) is a non-linear problem and iterative in two levels. Therefore, the [STOP](#) line changes to have five entries: an integer, a real value, a character, an enforcing character “**f**” and an integer. Now the first integer value gives the maximum number of [PCG](#)-iterations within each NR- or EM-round (default is 100 or number of equations in the MME) and the last integer value gives the maximum number of NR- or EM-rounds (default is 5000). Analyse is set to be converged when only one [PCG](#) iteration round is needed within the NR round, or less than 10 [PCG](#) iteration rounds are needed within the EM round.

There should be insignificant differences in solutions between two algorithms, but the EM algorithm is generally slower to converge than NR algorithm. NR algorithm is critical to attain good solutions within the rounds. Increasing the maximum number of [PCG](#)-iterations within each round may lead to fewer NR rounds and in that way faster convergence finally. Instead, EM algorithm will need reasonable solutions to certain

extent within each EM round, after which increase in accuracy will not improve the total convergence.

### 8.1.3 Solution files

Solution files are equal to the linear mixed model case. When thresholds are estimated, these are printed in the output and in the end of the `Solfix`-file (with factor name Threshold and factor number 0).

### 8.1.4 Example

[Example 7.9](#) in *Technical reference guide for MiX99 pre-processor* contains the instruction file for bivariate model with one binary trait.

## 8.2 Gompertz-model

A multiplicative Gompertz model (i.e.  $\ln(y) = \ln(a) - b * \exp(-k * t) + e$ ) as demonstrated in [Vuori et al. \(2006a\)](#); [Vuori et al. \(2006b\)](#) is implemented in MiX99. Thus, log-transformation is needed for original observations  $y$ , although solutions are for three parameters  $a$ ,  $b$  and  $k$ . All traits introduced in the analysis must currently have the non-linear Gompertz form. Models are allowed to have [missing traits](#) and unequal design matrices for traits. (Co)variance components could be known or estimated simultaneously between each round by the covariance component estimation program which allows linear random regression models.

### 8.2.1 Instruction file for `mix99i`

Model specification for non-linear model reminds the specification of regression models, although few additional features and restrictions compared to model specification for linear random regression traits exist. The two most important lines in the [instruction file](#) therefore are `MODEL` and `REGRESS` lines which will be discussed below.

Non-linear Gompertz-model traits are defined in the `MODEL` line by giving the character **G** on its own column between first and second parameters. Effects in the `MODEL` lines are defined as many times as number of parameters of the Gompertz function the effect is related to (i.e. 1-3 times for Gompertz function, see [example 7.8](#)). However, for all traits, at least one common fixed effect needs to be related to all three parameters. This effect is defined first in the `MODEL` line, and further, is defined to be across-block effect (see [WITHINBLOCKORDER](#)). I.e., dash (-) must be specified for the first effect in `WITHINBLOCKORDER` line. If many such effects occur, you may define effect with smallest number of levels first.

All factors in the `MODEL` line must be considered as covariables read from the separate file, i.e., covariable columns have to be specified with a preceding "t" on the `REGRESS` line(s). Real input column for covariable indicates the parameter of the Gompertz function the effect is related to: **t1** for mature weight, **t2** for relative initial weight and **t3** for maturation rate. An additional column for time is needed at the end of each `REGRESS` line. This is not counted in the number of regression effects specified first in the `REGRESS` line.

In consequence, a covariable file is always needed. The index connecting an observation and a set of covariables is usually time of measurement but the rest of the file

differs from those to linear random regression models. Because the Gompertz function has three parameters, first three covariable columns should contain only ones. After these, a column with the time variable is set. This can also be a scaled time if needed. E.g. select time scaling so that estimate for maturation rate is approximately one. The number of columns needed in covariable table is therefore at least 4, i.e., number of parameters in the non-linear Gompertz function plus one for the time dependent.

Addition to **MODEL** and **REGRESS** lines, restrictions on **PRECON** and **DATASORT** lines should be mentioned: (1) Diagonal (d) must be defined for all **preconditioners** and (2) multiple residual (co)variance matrices are not possible for non-linear Gompertz function models.

Note: The iterative algorithm for non-linear Gompertz function model is implemented so that a restart of analysis is needed. For this reason the user must define the convergence of the iterative process by itself. However, this enables the possible update of new variance components for each iteration round by calling **mix99i** first. Therefore both options in the **SOLUNF** line are possible, but restart of **mix99s** is possible with option **n** as well in case the covariance components are known and won't change from round to round. The case when estimation of variance components is done simultaneously is covered in the section of stopping criteria file.

### 8.2.2 Stopping criteria file for **mix99s**

Stopping criteria file is defined as for linear traits. Now the stopping criterion is for BLUP solutions within each round. To decide the final convergence of the iterative process, user must define the convergence by itself over repeated BLUP analysis. One option would be to append the solutions after each round to another file which is studied for converge of solutions.

It is possible to estimate variance components simultaneously between each round by another analysis. This is allowed by the option **d** in **SOLTYP** line, which will produce binary and ascii files named **DMUINP** and **DMUINP.dat**, respectively. There is a historical reason for naming files according to DMU, but any other suitable program can be used also. These files include the pseudodata, i.e., linearized observations and covariables, among others. **Missing observations** and **covariables** in **DMUINP** and **DMUINP.dat** files are coded as -99999. First within these files are integer columns and then real columns. Integer columns contain within and across block fixed effects and random non-genetic and genetic effects, in this order. After these there is the column with zeros. First real columns contain linearized observations for each trait, after which linearized covariables for each three Gompertz function parameters by traits follow. Last real column contain ones. Note: Good knowledge and carefulness is needed to estimate the covariance components accurately.

### 8.2.3 Solution files

Program gives solutions for Gompertz-model parameters (i.e.  $a$ ,  $b$  and  $k$ ) defined for each effect. Because model mimics linear random regression model, solutions files are equal to the linear random regression model case.

#### 8.2.4 Example

Example 7.8 in *Technical reference guide for MiX99 pre-processor* contains the instruction file for Gompertz function.

## 9 Estimation of variance components

For prediction of breeding values, variance components need to be known. An implementation of the Monte Carlo (MC) Expectation Maximization (EM) Restricted Maximum Likelihood (REML) (MC EM REML) algorithm for the estimation of variance components ([Matilainen et al., 2012](#)) is now available in the `mix99s solver`. The algorithm applies a resampling procedure to estimate prediction error variances (PEV) needed in the EM REML equations. Estimates of location parameters are obtained from the real data within each REML round, whereas PEV is obtained within each REML round by repeatedly simulating data and estimating the location parameters of the simulated data. This enables calculation of PEV without inversion of the coefficient matrix, leading to memory requirements equal to the solving of the mixed model equations. Although EM algorithm is known to be slow in convergence, the MC EM REML makes REML feasible for large data sets and complex models for which the inversion of the coefficient matrix would be too memory and time consuming.

The implementation for the variance component estimation supports the majority of models possible in **MiX99**. However, analysis of models which include an external correlation structure matrix (e.g. an IBD matrix), or which include an effect with an autoregressive correlation structure as well as [threshold models](#) and [Gompertz models](#) are not supported yet.

The current implementation has been developed and tested to serve an ongoing research co-operation between Luke (former MTT) and Rothamsted Research (UK). We consider this implementation ready to be tested by MiX99 users as well. Any feedback about your experiences is very much appreciated.

Instructing **MiX99** to estimate variance components will require information in three different files, which will be explained in the following.

### 9.1 File with (co)variance components starting values (PARFILE)

The file with the starting values for the (co)variance components must be in the same format as described in the chapter [File with \(co\)variance components](#) of the *Technical reference guide for MiX99 pre-processor*. The file will be specified in the **PARFILE** instruction line of the **CLIM command file** or MiX99 [instruction file](#). The same rules apply also for a file with starting values for the multiple residual (co)variance matrices in the case that a model with multiple residual (co)variances is applied (optional).

### 9.2 MiX99 instruction file

There is no need to give a specific instruction neither in the MiX99 [instruction file](#), nor in the **CLIM command file** when variance component estimation is desired. However, in the case that the `mix99i` pre-processor will be instructed by a MiX99 [instruction file](#), then the MiX99 [instruction file](#) must be named `MiX99_DIR.DIR`. This is because during developing of the variance component estimation module it was anticipated that the majority of analyses will be instructed by a **CLIM command file**, which in turn instructs `mix99i` to create a `MiX99_DIR.DIR` file automatically. This file is needed during the variance component estimation.

In the currently implemented version of the variance estimation module the `mix99s` solver will automatically, in certain `REML` round intervals, make a system call to start a `mix99i` pre-processing run, which will update the preconditioner matrices with the most current variance component estimates. For that reason the `MiX99_DIR.DIR` file will be need. Updating of the `preconditioner` matrices was found crucial to enhance convergence. The updating is done every 10<sup>th</sup> `REML` round during the first 100 `REML` rounds and on every 100<sup>th</sup> `REML` round thereafter. If the updating did not succeed, the text

```
1 Preconditioner has not been updated.
```

and either

```
1 File MiX99_DIR.DIR not found.
```

or

```
1 Check the file MiX99_DIR.LOG.
```

is printed to the standard output.

### 9.3 MiX99 solver option file

The `mix99s` solver is instructed to estimate variance components by specifying option `e` on the `VAROPT` option line and by giving information on three additional option lines thereafter. How to specifying the information on three additional option lines is explained in chapter 4.1 regarding the option `e` (*estimation of variance components*).

The stochastic `MC EM REML` implementation requires specifying of the *number of data samples* generated and analyzed within a `REML` round (given on the option line `STOPE`). The number of analyzed data samples within a `REML` round will affect the accuracy of the prediction error variance estimates. Increasing the number of samples will reduce the Monte Carlo error associated with the prediction error variances. However, the size of Monte Carlo error depends also on the model specified and on the amount of data and animals include in the analysis.

We observed that convergence of the `MC EM REML` algorithm is not affected by the number of samples specified and for many models even one sample per `REML` round is sufficient. The number of specified data samples is critical, because each additional data sample will require one additional BLUP model to be solved within a `REML` round, which increases the total time of the `REML` analysis.

From experiences made up to now, we propose for analysis with large amount of data and sufficient number of animals (e.g. test-day data with observation from over 10 000 animals) to specify one sample only. For analysis where amount of data is rather little, in relation to the number of parameters to be estimated, a higher number of samples (5, 10 or 20) might be more appropriate. For some analyses with very small amount of data, one might consider whether software with an analytical `REML` implementation is more suitable.

#### 9.3.1 Keeping certain variance components fixed

For some analyses it might be desired that certain pre-defined variance components (starting values) remain unchanged during the `MC EM REML` analysis. The instruc-

tions about which variance component parameters are kept fixed are given in the MiX99 [solver option file](#).

For this option the three entries **e f n** have to be specified on the **VAROPT** option line, where **f** instructs **mix99s** to keep some parameters unchanged and the third entry **n** is an integer value which tells how many parameters should remain unchanged. This option will require the inserting of **n** additional lines right after the **VAROPT** line. Each line specifies one parameter that should remain unchanged. A line consists of three integers, where the first integer is the random effect number followed by the row-column combination. In practice, you can copy the corresponding line from the parameter file excluding the variance component parameter itself.

In case [multiple residual variance matrices](#) are applied, four integers need to be defined for residual variance component parameters which should be kept unchanged. The first integer number is equal to the random effect number of the residual effect. The second integer gives the residual variance class number. This is equal to the first number on the corresponding parameter line in the file with multiple residual (co)variances (see chapter 3.4 in [Technical reference guide for MiX99 pre-processor](#)). And the last two integers specify the row-column combination.

## 9.4 Determining convergence of REML parameter estimates

There is a need for a [convergence indicator](#) which accounts for the characteristics that parameter estimates are associated with Monte Carlo noise. The currently implemented convergence indicator is calculated from the vectors containing predicted variance component estimates at two points  $x - 1$  and  $x$  ( $\hat{\mathbf{s}}(x - 1)$  and  $\hat{\mathbf{s}}(x)$ ), where the prediction is based on estimated variance components obtained during the latest  $x$  EM rounds ( $\hat{\boldsymbol{\theta}}^{(k-x+1)}, \dots, \hat{\boldsymbol{\theta}}^{(k)}$ ), and where a predicted estimate for each variance parameter is calculated as  $\hat{s}_i(x) = \hat{\alpha}_i + \hat{\beta}_i x$ . The size of  $x$  is chosen to be large enough to minimize the Monte Carlo noise in the [convergence indicator](#), which is calculated for REML round  $k$ :

$$cc_E^{(k)} = \frac{(\hat{\mathbf{s}}^{(k)}(x) - \hat{\mathbf{s}}^{(k)}(x - 1))^T (\hat{\mathbf{s}}^{(k)}(x) - \hat{\mathbf{s}}^{(k)}(x - 1))}{(\hat{\mathbf{s}}^{(k)}(x))^T (\hat{\mathbf{s}}^{(k)}(x))}$$

After  $cc_E^{(k)}$  has reached a value smaller than the specified convergence criterion (see **STOPE** option line), the **REML** analysis will perform a sequence of 30 additional **MC EM REML** rounds, which will eliminate the Monte-Carlo error from the parameter estimates by using weighted average with decreasing weights for latest solutions. So far, depending on the analysis, it was found that values between 1.0e-8 to 1.0e-9 are suitable convergence criterions.

## 9.5 Standard errors for REML parameter estimates

MiX99 is capable to calculate standard errors for the variance component estimates at the last REML round. Approximated standard errors are based on variances over sampled gradients as explained for NR-method in [Matilainen et al. \(2013\)](#). They are calculated automatically when the [number of data samples](#) is at least 10. Adequate number of samples depends on the data and model, but 50 or more samples is recommended. If less than 10 data samples are used to estimate the (co)variance parameters, one

## TECHNICAL REFERENCE GUIDE FOR MIX99 SOLVER

additional REML round could be done afterwards with larger number of samples. In that case, two changes are needed. First, change **PARFILE** in the instruction file to be **parfile** of previous run. Second, change maximum number of REML rounds to be one and number of data samples to be for example 50 in the solver option file.

Approximated standard errors, as well as all covariances of REML estimates in the information matrix, are printed after the last REML round. Standard errors are printed to the **vceSE**, and information matrix is printed to the **vceI**. The **vceSE** has four columns. It resembles the **parfile**, but has approximated standard errors in the fourth column. If model has **multiple residual variance matrices**, standard errors for all residual classes are printed after the first residual class (like in **REMLlog**). Example about **vceSE** is for one trait with two random effects and residual:

### **vceSE:**

1	1	1	1	208.134
2	2	1	1	272.508
3	3	1	1	59.4737

The **vceI** has seven columns. First three integers indicates the first parameter and the next three integers indicates the second parameter. Seventh column has the covariance between the two parameters. For example above, **vceI** is

### **vceI:**

1	1	1	1	1	1	1	43319.7
2	2	1	1	1	1	1	-44735.8
3	2	1	1	2	1	1	74260.4
4	3	1	1	1	1	1	-1222.08
5	3	1	1	2	1	1	485.008
6	3	1	1	3	1	1	3537.12

The information matrix contains a value for each combination of the (co)variance parameters and so it becomes large very soon. For example, for model with six (co)variance parameters, the information matrix contains 21 elements.

### **vceSE:**

1	1	1	1	98919.7
2	1	2	1	3534.95
3	1	2	2	155.895
4	2	1	1	82881.3
5	2	2	1	2914.91
6	2	2	2	126.006

### **vceI:**

1	1	1	1	1	1	1	0.978512E+10
2	1	2	1	1	1	1	0.310664E+09
3	1	2	1	1	2	1	0.124959E+08
4	1	2	2	1	1	1	0.987140E+07
5	1	2	2	1	2	1	483421.
6	1	2	2	1	2	2	24303.1
7	2	1	1	1	1	1	-0.755926E+10
8	2	1	1	1	2	1	-0.238666E+09
9	2	1	1	1	2	2	-0.741774E+07
10	2	1	1	2	1	1	0.686931E+10
11	2	2	1	1	1	1	-0.236382E+09
12	2	2	1	1	2	1	-0.937649E+07
13	2	2	1	1	2	2	-355953.

14	2	2	1	2	1	1	0.216383E+09
15	2	2	1	2	2	1	0.849670E+07
16	2	2	2	1	1	1	-0.737152E+07
17	2	2	2	1	2	1	-356791.
18	2	2	2	1	2	2	-17917.6
19	2	2	2	2	1	1	0.667658E+07
20	2	2	2	2	2	1	319118.
21	2	2	2	2	2	2	15877.5

For model with 42 (co)variance parameters, the information matrix contains as much as 903 elements.

## 9.6 Solution files for variance components

**REMLlog** Contains the estimates of variance components at every REML round. The first column in the file specifies the REML round, after which as many columns follow as there are variance component parameters to be estimated. The order of the lines is as following. The first three lines in the REMLlog describe the order of the parameter columns of which the first line contains the random effect number and the second and third lines the row-column combination for the particular parameter of a random effect. Hence, the first three lines are identically with the first three columns in the file with the (co)variance components. If multiple residual variance matrices are defined, then their variance class number is added to the end of the file. The fourth line contains the initial parameter values used. The following lines contain the estimates of variance components at each REML round.

**parfile** Contains the latest solutions of variance component estimates. The structure of the file is the same as in the parameter file of the PARFILE instruction line.

**resfile** Contains the latest solutions of residual variance component estimates when multiple residual variance matrices are defined. The structure of the file is the same as in the multiple residual variance matrices file of the RESFILE instruction line.

**vceSE** This file will be produced when approximated standard errors for REML parameter estimates are calculated. Resembles parfile. First three integers indicates the random effect number and row-column combination of that matrix. Fourth column contains the real value and is approximated standard error. If the model has multiple residual variance matrices, these are numbered as in REMLlog and printed right after the standard errors for other random effects.

**vceI** This file will be produced when approximated standard errors for REML parameter estimates are calculated. The file has seven columns. Seventh column has the value of the information matrix for each pairwise parameter combination. The first parameter is indicated by the first three integers as in vceSE, and the second parameter is indicated by the next three integers as in vceSE.

## 9.7 Example

Schaeffer has written a technical note on maximum likelihood estimation of variance components (Journal of Dairy Science, 1976). It contains a small example data in Table 1 for milk yields of first lactation daughters of five dairy sires in two herds. The model contains sire groups and herds as fixed effects and uncorrelated sires as random effects. In the following the [CLIM command file](#) for the `mix99i` pre-processor and the MiX99 [solver option file](#) for the `mix99s` solver program, as well as the listing in the standard output of the solver are given.

### **CLIM command file:**

```

1 TITLE data in technical note of Schaeffer (Table 1, J. Dairy Sci., 1976)
2
3 DATAFILE data.dat
4 INTEGER group herd sire
5 REAL yield
6
7 PARFILE data.par
8
9 PEDFILE data.ped
10 PEDIGREE sire sm
11
12 MODEL
13 yield = group herd sire

```

### **The “`MiX99_DIR.DIR`” file created for `mix99i`:**

```

1 # TITLE data in technical note of Schaeffer (Table 1, J. Dairy Sci., 1976)
2 data in technical note of Schaeffer (Table 1, J. Dairy Sci., 1976)
3 # INTEGER group herd sire
4 group herd sire
5 # REAL yield
6 yield
7 # TRAITS
8 1
9 # TRAITGRP
10 1 -
11 # datasort: Block_code, Relationship_code
12 - -
13 # FIXRAN: Numbers of fixed and random factors in the model
14 2 1 0 0
15 # MODEL: Subgr. Trait Weight ... model factors ...
16 1 1 - 1 2 3
17 # WITHINBLOCKORDER: Order of effects within blocks
18 - - 1
19 # RANDOM
20 1
21 # RELATIONSHIPS
22 1 1
23 # REGRESS
24 3 cl cl cl
25 # COMBINE
26 n
27 # PEDIGREE
28 sm
29 # DATAFILE data.dat
30 data.dat
31 # VAR
32 3 1 f
33 # MISSVA
34 0
35 # SCALE
36 n

```

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

```

37 # PEDFILE data.ped
38 data.ped
39 # PARFILE data.par
40 data.par
41 # tmpdir
42 .
43 # noransol
44 Y
45 # SOLUNF
46 n
47 # precon
48 b b # Default is block
49 # parallel: Number of processors used by the solver program
50 1 # Default: no parallel computing
51 # COMMONBLOCKS: Number of blocks in common area for parallel computing
52 0

```

### MiX99 solver option file:

```

1 # RAM: RAM demand: H=high, M=medium, L=low
2 H
3 # STOP: Max. num. iterations, Stopping criterion, Convergence indicator, enforce
4 5000 5.0e-5 d f
5 # RESID: Calculate residuals? (Y/N)
6 N
7 # VALID: N=none, P=prediction, S=sum of effects, Y=YD, D=DYD, I=IDD
8 N
9 # VAROPT: adjust for heterogeneous variance (N, E, S, C)
10 E
11 # STOPE: REMLrounds, nSamples, stopCritVCE
12 100 5 1.0e-9
13 # SEED: Type of seed for the random number generator
14 R
15 # MIX99PATH:
16 /share/apps/
17 # SOLTYP: type of solution files? (Y,N,A,H)
18 Y

```

### Standard output file of the solver at each REML round (comments after # are added):

```

1 .
2 .
3 -----
4
5 MiX99_SOLVE: Start of Iteration           Time:   10:55:34.824   04. 08. 2010
6 -----
7
8           Iteration Statistics
9           -----
10
11          Convergence Criteria
12          -----
13
14 ROUND      CA           CR           CD           MAX.CHA.
15 -----
16
17 Solution vector will be initialized with old solutions # Solutions from the
18                                                         # previous round used
19      rhs' * rhs =      2971967.58364948
20 animal rhs' * rhs =      497354.525482828
21 -----
22      0      0.2791E-02      0.1142E-02      0.000      0.000
23      1      0.5602E-04      0.3680E-03      0.8788E-02      0.4010E-01
24      2      0.1949E-03      0.1558E-03      0.1071E-02      0.4419E-02
25      3      0.4230E-04      0.4014E-04      0.1754E-03     -0.4271E-03
26      4      0.1339E-03      0.6118E-04      0.4087E-03      0.1175E-02
27      5      0.1455E-03      0.8434E-04      0.1496E-02     -0.4730E-02
28      6      0.5961E-05      0.3908E-05      0.2639E-02     -0.7985E-02

```

# TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

```

29      7      0.2349E-04      0.9748E-05      0.2413E-03      0.7708E-03
30      8      0.1987E-15      0.1915E-15      0.2923E-03      0.8160E-03
31      9      0.3667E-17      0.2831E-17      0.2231E-15      0.4441E-15
32
33      Solutions converged after          9 iterations.          # Convergence of real data
34
35
36
37
38 MiX99_SOLVE: End of Iteration          Time:    10:55:34.837    04. 08. 2010
39
40
41  9  0.9642E-15  0.9866E-15  0.4228E-14 -0.2165E-14  # Solutions for 1st simulated data
42  9  0.3743E-16  0.4106E-16  0.2478E-12  0.6847E-13  # Solutions for 2nd simulated data
43  9  0.8067E-15  0.1105E-14  0.1197E-13  0.4885E-14  # Solutions for 3rd simulated data
44  9  0.6588E-14  0.6372E-14  0.7982E-13  0.2370E-13  # Solutions for 4th simulated data
45  9  0.1554E-14  0.1423E-14  0.7645E-12  0.3822E-12  # Solutions for 5th simulated data
46
47 REML ROUND          11  CONV Cd    1.212191543865694E-003  # Convergence indicator
48 .
49 .

```

## 10 Accounting for heterogeneous variance

The need to account for heterogeneous variances (HV) in several dairy cattle evaluations led to the implementation of this possibility into *MiX99*. The applied method is based on the multiplicative mixed model (MMM) approach given in [Meuwissen et al. \(1996\)](#). The approach requires to solve simultaneously the model for breeding value estimation ([mean model](#)) and a model for dispersion parameters ([variance model](#)). For our needs, to accommodate multiple trait test-day models, we have modified the approach of [Meuwissen et al. \(1996\)](#). The most important modifications are: scaling factors are standardized to keep the across trait covariance structure unchanged; loss in degrees of freedom due to the estimation of fixed effects in the [mean model](#) is accounted (by an approximation) for the estimation of residual variances within strata; variance components for the [mean model](#) are not re-estimated; and the solving algorithm was modified to allow large test-day models. A description of the implemented method is given in [Lidauer et al. \(2008\)](#).

The implementation was targeted towards test-day models for dairy cattle. This required some restrictions on the variety of [variance models](#) that can be fitted. However, the current implementation should allow accounting for [heterogeneous variance](#) in many other models beside test-day models. However, [non-linear models](#) are not supported.

For future versions of MiX99 we target on a larger variety of [variance models](#) and simplified implementation.

### 10.1 Computation environment

The current implementation works only for the [parallel](#) solver in *MiX99*. Therefore, a MPI (message passing interface) environment is required on the computing platform. The HV method was implemented having shared memory computer architecture in mind. However, meanwhile we have implemented the HV method also on distributed memory platforms. An example of the required scripts for setting up the HV method on a distributed memory platform (Linux-cluster) may be requested from the authors.

### 10.2 Models for the heterogeneity of variances

In the [multiplicative mixed model](#) approach two models have to be solved simultaneously, the mean model (the model with the breeding values) and the variance model (the model, which describes the heterogeneity of variances). By definition of the [multiplicative mixed model](#) approach, the [mean model](#) must be nested within the [variance model](#). This is because scaling of observations of a particular stratum will change the mean of these observations, which requires that the [mean model](#) is able to account for this change.

#### 10.2.1 Currently supported *variance models* by MiX99

For large models, like random regression test-day model, solving a multiplicative model is a challenging task. Therefore, some restrictions were necessary on the type of [variance models](#) that can be fitted. The possibility for a larger variety of [variance models](#) would lower computation speed, and therefore, is not implemented yet. For an easier understanding, a short explanation of the computations is given:

Considering a **mean model** of the form:

$$\mathbf{y}_i \lambda_i = \mathbf{X}_i \mathbf{b} + \mathbf{Z}_i \mathbf{a} + \mathbf{e}_i$$

where,  $\mathbf{y}_i$  contains all observations of stratum  $i$ , which are scaled with the same adjustment factor  $\lambda_i$ ; and a **variance model** of the form:

$$s_{ik} = \beta_{1_{ik}} + \beta_{2_{ik}} + \epsilon_{ik}$$

where  $\beta_{1_{ik}}$  is a fixed effect and  $\beta_{2_{ik}}$  may be a fixed or a random effect.

Solving of the **MMM** of those two models will follow the approach given in [Meuwissen et al. \(1996\)](#) apart from a few modifications. The solving scheme starts with the initialisation (I step). In the following, step P, E, M, and A will be cycled until the adjustment factors are sufficiently converged. Finally, step P will be performed until solutions to the **mean model** are converged. The steps are:

**I step:**  $q = 0, \lambda^{[q]} = 1, \beta^{[q]} = 0, \text{ and } \sigma_{eT}^{2[q]} = \sigma_{eT_{MMM}}^2$

**P step:**  $\mathbf{y}_{cT_i}^{[q]} = \mathbf{y}_{T_i} \lambda_{T_i}^{[q]}$  and iterate **mean model**

**E step:**  $\hat{z}_{T_i}^{[q]} = 0.5 \left[ \mathbf{y}_{cT_i}'^{[q]} \left( \mathbf{y}_{cT_i}^{[q]} - \hat{\mathbf{y}}_{cT_i}^{[q]} \right) \sigma_{eT}^{-2[q]} - n_{T_i} \right]$  [3]

$$\hat{w}_{T_i}^{[q]} = 0.25 \sigma_{eT}^{-2[q]} \mathbf{y}_{cT_i}'^{[q]} \hat{\mathbf{y}}_{cT_i}^{[q]} + 0.5 n_{T_i}$$
 [4]

$$s_{T_i}^{[q]} = \left( \hat{z}_{T_i}^{[q]} / \hat{w}_{T_i}^{[q]} \right) + \beta_{1_{T_i}}^{[q]} + \beta_{2_i}^{[q]} - \beta_{T_{BASE}}^{[q]}$$
 [5]

**M step:** iterate  $[\mathbf{S}' \mathbf{W}^{[q]} \mathbf{S} + \Delta \nu] \beta^{[q+1]} = \mathbf{S}' \mathbf{W}^{[q]} \mathbf{s}^{[q]}$  [6]

**A step:**  $\lambda_{T_i}^{[q+1]} = \exp \left[ -0.5 \left( \beta_{1_{T_i}}^{[q+1]} + \beta_{2_i}^{[q+1]} - \beta_{T_{BASE}}^{[q+1]} \right) \right]$  [7]

$$\sigma_{eT}^{2[q+1]} = \sigma_{eT}^{2[q]} \exp \left( \beta_{T_{BASE}}^{[q+1]} \right)$$
 [8]

where  $q$  is the adjustment cycle;  $\sigma_{eT}^2$  is the standardization variance for trait  $T$ ;  $\sigma_{eT_{MMM}}^2$  is the residual variance for the trait  $T$  used in the **mean model**;  $\mathbf{y}_{cT_i}$  includes the adjusted observations for trait  $T$  and stratum  $i$ ;  $\hat{z}_{T_i}$  is an estimate of the heterogeneity of the residual variance for trait  $T$  in stratum  $i$ , and  $\hat{w}_{T_i}$  is the variance of  $\hat{z}_{T_i}$ , where  $\hat{\mathbf{y}}_{cT_i}$  is the prediction of  $\mathbf{y}_{cT_i}$ , and  $n_{T_i}$  is the number of observations for trait  $T$  in stratum  $i$ ;  $s_{T_i}$  resembles the observation for the **variance model** related to trait  $T$  in stratum  $i$ ;  $\beta_{T_{BASE}}$  is the weighted mean of the  $\beta_{1_{T_i}}$  estimates that built the base for trait  $T$ ;  $\mathbf{s}$  contains all  $s_{T_i}$ ,  $\beta$  contains all  $\beta$  estimates and  $\mathbf{S}$  is the corresponding design matrix;  $\mathbf{W}$  is diagonal with all  $\hat{w}_{T_i}$  estimates at the diagonal, and if desired,  $\Delta \nu$  may present a variance structure (i.e. autoregressive process) for random effect  $\beta_2$ .

The current version has the following requirements for the definition of the **variance model**:

- 1) The **variance model** must have the same number of traits as the **mean model**. In case of a multiple trait model, because of computational reasons, traits are analyzed simultaneously even the traits are uncorrelated.

- 2) If traits are grouped by trait groups, traits must be grouped in the same order in both models.
- 3) Two effects must be specified for each trait.
  - ⇒ *Fixed across block strata*: The first effect must be a fixed effect. Usually this effect will describe heterogeneity of variance between strata, which is common across the whole data; for instance, strata like years, seasons, parities, etc.
  - ⇒ *Fixed/random within block strata*: The second effect may be a fixed or a random effect. In case of a fixed effect, please see [MODEL](#) instructions, about how to specify LS-models. In case that the second effect is random, optionally, a [first order autoregressive process](#) for strata within same environments (blocks) is supported. For the latter, a program ([mix99hv](#)) is provided, which sets up the autocorrelation structure.

The previous three requirements for the [variance model](#) should be easy to accommodate. However, there is one more restriction on how the strata for the two effects in the [variance model](#) must be defined. These restriction are because of computational constrains only. For an easier understanding of this restriction it is worth to know that [mix99p](#) performs all calculations of step E for one data block at the time. For the need of fast computations all required information is stored in vectors, rather than in linked lists. To avoid exhaustion of computer memory only the segment of the strata that relates to one data block is made accessibly during processing of a particular data block. This causes the following two restrictions:

- 1) The second effect ( $\beta_2$ ), regardless whether it is defined as fixed or as random, must include a block interaction. The block structure must correspond with the block structure of the [mean model](#). Note: The blocking variable of the [mean model](#) will be included as interaction in the second effect of the [variance model](#) in the form block  $\times$  within-block classes (see [10.3.1](#)). Therefore, it is important that the blocking variable in the [mean model](#) is the same for all observations with the same production environment. For instance in dairy cattle, the blocking variable may be herd of production, but it must not be herd of birth, if [heterogeneous variance](#) due to different production environments should be adjusted. Calculations are performed in block-wise manner, where a data block in the [mean model](#) has a corresponding data block in the [variance model](#). This requires, that each stratum of the second effect can only be present in one block.
- 2) Strata of the first effect ( $\beta_1$ ) can be associated with data of different blocks. However, because of computational restrictions, within each data block a strata of the first effect ( $\beta_1$ ) can only be associated with one strata of the second effect ( $\beta_2$ ). Thus, the levels of the first effects must be nested within the levels of the second effect. (This is because within each block only one pointer to the second effect strata is stored for each first effect strata. The restriction could be relaxed if a pointer to the second effect strata would be stored for each observation. However, this would be currently computationally too expensive). Different strata of the first effect can be associated with the same stratum of the second effect. For instance, if the first effect in the [variance model](#) is a *region $\times$ year $\times$ season* effect, then the second effect may be a *herd* effect, a *herd $\times$ year* effect, or a

*herd*×*year*×*season* effect. However, if the first effect is a *year* effect only, then the second effect may not be a *herd*×*year*×*season* effect.

### 10.3 Input data for the variance model

The program `mix99hv` sets up the required input data files for the [variance model](#). In order to get first heterogeneity observations, a few iterations have to be made on the [mean model](#) prior to the `mix99hv` run.

#### 10.3.1 Input data for `mix99hv`

Three integer columns of the input data file for the [mean model](#) are read by `mix99hv` when setting up the data file for the [variance model](#). These three columns are: the column for the blocking variable, a column with the strata of the first effect of the [variance model](#), and a column with the [within block strata](#) for the second effect of the [variance model](#). The blocking variable must be consistent with the production environment in which the observations were made. For instance, herd of production but not herd of birth. This is important because `mix99hv` uses the blocking variable for coding the second effect of the [variance model](#). For the same reason, the third column must contain a within-block stratification only (without block interaction).

Both columns, that one with the blocking variable and the other one with the within-block stratification, are used to set up information for the first order autoregressive process (Wade and Quaas, 1993) and to set up the strata for the second effect in the [variance model](#). To accommodate the autocorrelation structure, coding of the within-block classes must be consistent with the distances between classes. When coding starts from  $n$  and goes up to  $k$ , then  $k - n$  is equal to the largest possible distance between classes of the block. Usually, classes are defined by the time when observations were recorded, e.g., year, month, week. Class codes have to be defined that the distance between consecutive classes is one, i.e,  $\text{class\_code } n+1 - \text{class\_code } n = 1$ . In case, there is a missing class between consecutive classes, the distance must be 2. It is advisable to number all possible classes consecutively from 1 to  $k$  and then give for each class the corresponding code. This way, `mix99hv` will automatically calculate the right distances between classes.

If the second effect in the [variance model](#) is considered as fixed effect or as a normal random effect, coding of the [within block strata](#) can be relaxed. However, in order to save memory requirements we recommend that within block, coding should be consecutively starting with one. Remember, that the actual class code for the second effect will be formed by the program `mix99hv` from the block sorting variable and the within block class code.

#### 10.3.2 Instruction file for `mix99hv`

Execution of `mix99hv` requires an instruction file, which is read by standard input. Editing rules for this file are the same as for the MiX99 [instruction file](#). The file contains several instruction lines, which have to be in the same order as given in the following. The file can contain as many comment lines as wanted.

**DATAFILE** The name of the input data file for the [mean model](#). If the data file is in a different directory, the whole path must be specified.

- VAR\_I** One line with one integer and one character. The integer is the number of integer columns in the data file. The character is a code for the type of the file.
- f** Formatted free format (columns are separated by at least one space).
  - u** Unformatted format, i.e., a binary file.
- TRGRP** One integer value that indicates the integer column with the trait group code in the data file. If trait groups are not needed the number must be set to zero (0).
- SORT\_B** One integer, which indicates the integer data column of the block sorting variable in the input data file for the [mean model](#). The variables in this column will be use to set up the [autocorrelation structure](#) and to form the class codes for the second effect in the [variance model](#) (see also [10.3.1](#)).
- MODVAR** One line with two integers. The first integer indicates the integer data column with the class variables of the first effect in the [variance model](#) (fixed [across block strata](#)). The second integer indicates the integer data column with the within-block class variables for the second effect in the [variance model](#) ([within block strata](#)).
- ARFILE** A line with one character. This character defines, whether a file ([AR.pedi.reml](#)) with information about the autocorrelation structure is created. This file is only useful for the estimation of variance components for the [variance model](#), using our tailored software, which is not included in MiX99.
- n** No. No file created.
  - y** Yes. File created.
- STAND** A line with one character. This character defines, whether or not standardization variances (provided in the file [HVbase\\_ResVar](#), for the calculation of the heterogeneity observations), should be scaled to result standardized adjustment factors, which are on average 1.0 for observations of the defined base strata. For more details, see [Standardization of the multiplicative adjustment factors](#). The Standardization process has to be done only once for a specific model. The obtained scaled standardization variances can then be used as parameters for future analyses.
- y** Yes. Standardization of multiplicative adjustment factors.
  - n** No. No standardization process.
- BASEFILE** If **y** is defined, an additional line with the name of the file, that contains the class codes for the base classes must be given (see [Standardization of the multiplicative adjustment factors](#)).
- APPROX** A line with one character for each trait. This character defines, whether or not rank approximation, to account for loss in degrees of freedom due to the estimation of fixed effects in the [mean model](#), should be considered for the estimation of within strata residual variances. This option was

included for the need to avoid an underestimation of within strata residual variances when size of strata is small. This approximation can only be used if within block fixed effect classes in the [mean model](#) match with the strata of the second effect in the [variance model](#). For instance, a fixed *herd×year* effect in the [mean model](#) and *herd×year* strata for the second effect of the [variance model](#). Otherwise, the loss in degrees of freedom will be underestimated.

- y** Yes. Consider rank approximation.
- n** No. Do not consider rank approximation.

**SETLOSS** One line with as many real values as there are traits in the model. This line is only given if **d** is specified at the end of the previous [APPROX](#) instruction line. Then, for each trait, for which rank approximation is not applied, a preset loss in degrees of freedom may be given. The value must be between 0.0 and 1.0.

**MERGE2** One line with as many integers as there are traits in the model. The integers tell whether or not strata of the second effect in the [variance model](#) are combined across traits. For the specification of the integers same rules apply as for one column in the [MERGE](#) instruction for `mix99i`. The specified integers must be consistent with the [MERGE](#) specification in the [variance model](#) instruction file. If combining is not desired integers from 1 up to n are given, where n is equal to number of traits.

**TMPHV** The directory where the HV information files `HV.data`, `HV.pedi`, `Lambda.data(i)`, `HV.info(i)`, and optional `ARsiwi.data(i)` will be created. These files are rather large and will be created during the execution of the script `runMMM`. If the HV information files should be in the same directory where the script is executed, a dot (.) is given.

### 10.3.3 Output files from `mix99hv`

The program `mix99hv` creates a file named `HV.data`, which is the input data file for the [variance model](#); a file named `HV.pedi`, which contains information about the autocorrelation structure; the files named `AR.block`, and `Hetlog`, which are read by `mix99i` and `mix99p`; as well as the files `HV.info(i)`, which are needed during updating of the adjustment factors.

#### **HV.data**

The file `HV.data` is created by `mix99hv` and is the input data file for the [variance model](#). The file is in unformatted (binary) format and contains integer and real data columns. First there are four integer data columns, followed by the real data columns, where the number of real data columns depends on the specified model.

Integer data column	Description
1	renumbered block sorting variable
2	renumbered class variables for the second effect
3	trait group code
4	renumbered class variables for the first effect

There are two groups of real data columns. The first group contains heterogeneity observations and the second group the corresponding weights for the heterogeneity observations. Each group has as many columns as there are number of traits in the largest trait group. E.g., if the first trait group includes two traits and the second trait group three trait, then there will be three columns for the heterogeneity observations and three columns for the weights. The order of the heterogeneity observations and of the weights follows the order of the traits within trait group. If there are fewer traits in a trait group, remaining columns are set to missing. If an observation is missing or if a column is not used for a certain trait group, a code for [missing values](#) will be given. This code is set to [-8192.0](#) and has to be given in the [instruction file](#) for the [variance model](#).

### HV.pedi

The file [HV.pedi](#) is created by [mix99hv](#) as well. The file is needed to provide the blocking information for the [variance model](#) and to set up the [autocorrelation structure](#) for second effect in the [variance model](#), if latter is desired. For the [variance model](#), the [HV.pedi](#) file replaces the normal pedigree file. The file has four integer columns:

Integer column	Description
1	renumbered class variables for the second effect
2	distance to the next classes
3	information about class position within block (1=first class in block; 2=class between; 0=last class in block; 3=first and last class in block)
4	renumbered block sorting variable

In case it is desired to define the second effect as a fixed effect ([LS-models](#)), information on column 2 and 3 will be not used. If the second effect should be a normal random effect, the autocorrelation parameters on the [RHO](#) instruction line should be set to zero (0.0) in the [instruction file](#) for the [variance model](#). This makes information on 2 and 3 redundant. Alternatively, it is possible to define instead of [ar](#) (autoregressive model) [am](#) (animal model) in the instruction file for the random model and set the values in column 2 and 3 to zero.

## 10.4 Instruction file for the variance model

Setting up the instruction file for the [variance model](#) follows the same rules as given for the [mean model](#). However, a large part of the instructions are already defined by the

general setup for the HV-adjustment. These pre-defined instructions are as following:

**TITLE**

**INT-VAR** Block BlockxCI Trg Fix

**REAL-VAR** Name of traits followed by weights for the traits. Names are in same order as given in the [mean model](#).

**TRAITS** Number of traits must be the same as in the [mean model](#).

**TRGRP** Number of trait groups must be the same as in the [mean model](#). Integer input column for the trait group code is 3.

**SORT\_R** 1 2  
The value 1 for the integer column with block code, followed by the value 2 for the integer input column of the second effect in the [variance model](#).

**FIXRAN** 1 1  
Two integers with the value 1, for the number of fixed and random factors.

**MODEL** As many model lines as there are traits in the model. Ordering of the traits within trait groups must be the same as in the [mean model](#). For the [variance model](#), all observations are weighted (see [Meuwissen et al. \(1996\)](#)). This requires defining of the real columns with the weights. In `HV.data`, the real columns with the weights start after the columns with the observations and have the same order as the columns for the observations. Note, if trait groups are defined, for any trait group, the column with the observations for the first trait within trait group is always the first real column. For each trait, the corresponding column with the weights is on position “size of largest trait group plus trait column”.

For the first effect in the [variance model](#) column 4 has to be defined, for the second effect column 2 (see Example 10.9).

**WITHINBLOCKORDER** - 1  
A dash (-) is given followed by the integer value 1.

**RANDOM** The second effect in the model has to be defined always as random (also for a [LS-model](#); see defining of [LS-models](#)).

**RELATIONSHIPS** 1 1  
Two integers with the value of 1.

**REGRESS** Only [class](#) variables (`c1`) are allowed.

**COMBINE** (`n/y`). In case `y` is given, then last column of the [MERGE](#) instruction lines must be consistent with the [MERGE2](#) line in the [instruction file](#) for `mix99hv`.

**PEDIGREE** `ar` for [autoregressive model](#), `am` for random effect, `ls` for [LS-model](#).

**RHO** In case `ar` is defined in [PEDIGREE](#), one line with as many autocorrelation values as there are traits in the model must be given. Order of the values must be the same as the order of traits. In case some traits are combined, the order of the

autocorrelations must follow the order of the corresponding variances that are applied for the last random effect.

- DATAFILE** The `HV.data` file is placed in the same directory as was defined for the work files in the [instruction file](#) for `mix99hv: /path for the work files/HV.data`.
- VAR** An integer value of 4 for the number of integer columns in `HV.data` followed by the number of real columns in `HV.data` and the character `u` for unformatted file. The number of real columns is two times the size of the largest trait group.
- MISSVA** `-8192.0`  
The code for missing heterogeneity observations is `-8192.0`.
- SCALE** `n`  
A `n` for no scaling.
- PEDFILE** The `HV.pedi` file is placed in the same directory as was defined for the work files in the [instruction file](#) for `mix99hv: /path for the work files/HV.pedi`.
- PARFILE** The name of the file with the variance components for the [variance model](#).
- TMPDIR** The directory where the temporary files for the [variance model](#) are placed. The directory must be a sub-directory of the directory with the temporary files for the [mean model](#) and must be named `B1: /path for the mean model temporary files/B1`.
- RANSOLFILE** `y`  
A `y` for the second effect in the model. In case of a [LS-model](#) a `y` must be given as well.
- SOLUNF** `n`  
A `n` for no unformatted solution files.
- PRECON** `d d`  
A `d` for the `WpW` and `d` for the `XpX` part, since all traits are uncorrelated.
- PARALLEL** Same number of processes as for the [mean model](#).
- COMMONBLOCKS** `0`  
An integer value of 0, because there is no common pedigree block in the model.

From release XII/2014 onwards the variance model can be given also with CLIM syntax. The following illustrates CLIM syntax needed to build variance model.

**Variance model CLIM:**

```

1 TITLE VARIANCE MODEL
2
3 DATAFILE BINARY path/to/HV.data
4 INTEGER BLCK HERDxYR TRGRP MONTH
5 REAL HET_OBS WGHT
6
7 MISSING -8192.0
8 TRAITGROUP TRGRP
    
```

```

9
10 DATASORT BLOCK=BLCK PEDIGREECODE=HERDxYR
11
12 PEDFILE path/to/HV.pedi
13 PEDIGREE HERDxYR ar
14
15 PARFILE variance_model.var
16 AR 0.7 # If pedigree type is ar then autocorrelation values
17 # for each trait must be given in AR statement
18
19 MODEL # As many model lines as there are traits in the model
20 # Ordering of traits must follow mean model!
21 HET_OBS(1) = MONTH HERDxYR ! WEIGHT=WGHT
22 # The first effect of the model is fourth integer column
23 # and the second effect is second integer column
24
25 PRECON d d
26 PARALLEL 2 0
27 WITHINBLOCKORDER HERDxYR

```

## 10.5 Variance components for the variance model

In case the second effect of the [variance model](#) is defined as a random effect, variance components are required. Estimation of the variance components depends on the specified model, and therefore, only a brief explanation about how variance components for the [variance model](#) may be estimated is provided. Generally, the estimation procedure requires first solving of the [multiplicative mixed model](#) followed by the estimation of variance components for the [variance model](#). The new variance components are updated in the [multiplicative mixed model](#) and the whole process is repeated until variance components do not change any more. *MiX99* authors will provide support for estimating VC for multiplicative mixed models.

At the moment the *MiX99* variance component estimation module does not support models with an auto-regressive correlation structure.

### 10.5.1 Files with information for the variance component estimation

For the estimation of the variance components, a file with the heterogeneity observations for the [variance model](#) is needed. *MiX99* provides the files named `ARsiwi.data(i)`, which contain the most recent heterogeneity observations plus the corresponding weights. The file is an unformatted file with real columns only. The order of the columns is the same as the order of the real columns in the `HV.data` file. The integer columns of the `HV.data` file and the real columns of the `ARsiwi.data(i)` files may be merged to create an input data file for the variance component estimation. In order to obtain the `ARsiwi.data(i)` files, an `h` must be specified in the [RESID](#) option line of the *MiX99* [solver option file](#) for the [mean model](#) (`Mean_model.slvM` in the `HV` directory).

In case, an autocorrelation structure is applied for the second effect in the [variance model](#), *MiX99* may provide two different files with the required information to set up the autocorrelation structure. The first is named `HV.pedi`, which contains the required information as needed for *MiX99*. The second is named `AR.pedi.reml`, and is created if a `y` is specified in the [ARFILE](#) instruction line of the [instruction file](#) for `mix99hv` (see [10.3.2](#)). The `AR.pedi.reml` file contains the following five integer columns:

Integer column	Description
1	renumbered class variables for the random effect ( <a href="#">within block strata</a> )
2	renumbered class variable for the next class of the random effect; this variable is zero (0) in case the class in the first column is the first or the last class of a block.
3	renumbered class variable for the next class of the random effect, in case the class in the first column is the first class of a block; and otherwise zero (0).
4	a column with zeros
5	a column with zeros

## 10.6 Standardization of the multiplicative adjustment factors

In the method presented by [Meuwissen et al. \(1996\)](#), variance components for the [mean model](#) are re-estimated, because accounting for HV has some effect on the heritability. However, re-estimation of variance components is hardly feasible for large models. Further, even it would be possible to extend the approach of [Meuwissen et al. \(1996\)](#) to multiple trait models, it would be computationally demanding. Therefore, in the current implementation, heterogeneity observations of different traits are considered to be uncorrelated in the [variance model](#). For all these reasons, a standardization procedure was implemented, which should assure that the covariance structure across traits remains unchanged.

The idea of the standardization procedure is to find for each trait a standardization variance  $var(s)$ , for which the quantity “  $[(\mathbf{y}'_i \mathbf{e}_i \lambda_i^2) / var(s)] - n_i$  ” becomes zero and the adjustment factors for observations in the base classes are on average 1.0;  $\mathbf{y}_i$  and  $\mathbf{e}_i$  are of size  $n_i$  and contain observations and residuals of stratum  $i$ , respectively;  $\lambda_i$  is the adjustment factor for stratum  $i$ . In a perfect world, the standardization variance  $var(s)$  would become same as the residual variance of the [mean model](#). The standardization variances have to be provided in a file named `HVbase_ResVar`. The file with converged standardization variances must be provided for any future (routine) runs.

### 10.6.1 Files for the standardization procedure

#### File with class codes of the base

The standardization base should include a part of the data for which it is reasonable to assume that standardization factors should be on average 1.0 for all traits. This part of the data must include observation from all traits (if this is not possible see [Standardization process](#)). Corresponding strata of the first fixed effect in the [variance model](#) need to be provided in the base class file. The file will be renumbered by `mix99hv` and original and renumbered class codes are written to `ID.Base`. The provided file may contain additional columns. The file `ID.Base` is repeatedly read by `mix99p` during the standardization process.

#### File with the residual variances

A file named `HVbase_ResVar` with as many rows as there are traits in the model. Each row corresponds to the trait in the model and contains the standardization variance. During the standardization process, the file will be updated after each adjustment cycle. The residual variances of the `mean model` can be given as starting values for the standardization process. The `HVbase_ResVar` file must be provided in the directory where `mix99p` is executed any time when adjustment for HV is considered.

### 10.6.2 Standardization process

The standardization process is specified in the `instruction file` for `mix99hv`. A `y` must be specified in the `STAND` instruction line, and on the `BASEFILE` line the filename of the file with the base class codes must be provided. To ensure converged standardization variances, we recommended a minimum of 150 adjustment cycles. Cycle to cycle changes in the standardization variances can be checked from the standard output file. The line marked with "Re:" contains the currently used standardization variances.

The provided standardization method might not work for very complicated models. For instance, if not all traits have observations in the same time period or in some cases where genetic effects are combined over traits. For such situations it is possible to keep the variance ratios between standardization variances of different traits unchanged. Providing the file `HVbase_ResVarLEVEL` will allow this task. The file has the same form as `HVbase_ResVar` but additionally a second column with integer values is included. The first column contains standardization variances and the integers in the second column specify which standardization variances should be altered and which should have a fixed ratio to another standardization variance. If the standardization variance is allowed to be altered, the own trait number is given. If the standardization variance should have a fixed ratio with the standardization variance of another trait, then the trait number of the other trait is given. For instance, if the standardization variance for trait two should be altered and the ratio between standardization variance for trait two and trait four should be fixed, then a 2 is specified for trait two and also for trait four.

### 10.6.3 Multiple residual variance-covariance matrices

Multiple residual variance-covariance matrices (see `Multiple residual (co)variances (RESFILE)` in *Technical reference guide for MiX99 pre-processor*) for the `mean model` are automatically considered for the calculation of observations for the `variance model`. However, for the standardization process one needs to be aware that provided standardization variances in the `HVbase_ResVar` file correspond to the residual variance-covariance matrix of the first residual variance class in the `mean model`. The base classes need to contain observations that go into the first residual variance class. During the standardization process, standardization variances for all other residual variance classes are automatically changed if the standardization variances for the first residual variance class are changed. The ratios between standardization variances of different residual variance classes are kept constant.

If it is desired that ratios between standardization variances of different residual variance classes are different from those between residual variances of different residual variance classes in the `mean model`, a file named `HVbase_ResVarCLASS` can be provided. The file has as many rows as there are multiple residual variance classes

and a many columns as there are traits in the model. Each row should contain the corresponding residual variances. For classes where higher or lower standardization variances are desired, the variances should be changed accordingly.

## 10.7 Running a model with heterogeneous variance

The applied [multiplicative mixed model](#) approach, to account for [heterogeneous variance](#), requires a simultaneous solving of two linear models, namely the [mean model](#) and the [variance model](#). Both models are solved by two different MiX99 runs, which interact with each other. To facilitate these interactions between the models a certain directory structure is required when setting up the models.

The [heterogeneous\\_variance](#) directory of the MiX99 package includes all required to set up to run a model with [heterogeneous variances](#). For distributed memory platforms, implementations are more complicated and we recommend a good understanding of the implementation for shared memory platforms before an implementation is done for a distributed memory platform.

### 10.7.1 Implementation on shared memory platforms

The [mean model](#) must be set up in an own directory. The [variance model](#) must be set up in a sub-directory of the [mean model](#) directory and must be named [B1](#). The directory with the temporary files for the [mean model](#) must be specified in the [instruction file](#) for the [mean model](#). The temporary files for the [variance model](#) must be in a sub-directory of the [mean model](#) temporary file directory and it must be named [B1](#). Additionally a third directory with [heterogeneous variance](#) information must be specified in the instruction file for [mix99hv](#). The input data files for the [variance model](#) will be placed into this directory. For large model, these three directories may require considerable amount of disk space.

The whole solving process is controlled by the script `runMMM` provided with MiX99 package. The script controls all required **MiX99** runs for solving the [multiplicative mixed model](#). The only required modifications in the script are to set the parameter for the number of processes ([PARALLEL](#)) and the calls to `mpirun`. The program `mix99p` calls the script `solve_HVmodel` during iteration process to start solving of the variance model. Output from this script is written to `CYC.log`

Three different solver option files are needed for multiplicative mixed model. The files in example provided are named as `Mean_model_init.slvI`, which is used to initialize mean model, solver option file `Variance_model.slvV` (in directory [B1](#)) for the variance model, and `Mean_model.slvM` for running the mean model. The convergence criterion for the adjustment procedure is given in the [STOPC](#) instruction line of the stopping criteria file `Mean_model.slvM`. From our experiences, a stopping criterion of  $1.0e-7$  for the relative change between adjustment factors of consecutive cycles or at least 80 adjustment cycles was found useful. However, a less conservative criterion may yield already sufficiently converged adjustment factors.

## 10.8 Workflow and needed files for running multiplicative mixed model

The following table shows all necessary files and directories needed to set up and run multiplicative mixed effects model. The filenames are the same as in HV example shipped with *MiX99*. Files that have to be named with a certain name are marked with a star (\*).

### Directory and file setup for multiplicative mixed model

#### Directories within mean model directory

*B1	Directory for variance model
tmpMiX	Directory for temporary files (Mean model)
*tmpMiX/B1	Directory for temporary files (Variance model). Should be a subfolder of mean model temporary files
tmpHV	Directory for HV information files (see <a href="#">TMPHV</a> )

#### Files

<a href="#">runMMM</a>	Script that does all steps
*B1/solve_variance_model	Script that runs variance model. Created by <a href="#">runMMM</a> script.
* <a href="#">solve_HVmodel</a>	Script called from <a href="#">mix99p</a> to run variance model. An example script is shipped with <i>MiX99</i> . Script runs B1/solve_variance_model

#### Files for Mean model

mean_model.[clm mix]	Definition for the mean model
mean_model.dat	Data
mean_model.ped	Pedigree
mean_model.var	Variance components for mean model
mean_model.resvar	Optional: Variance components for residuals if more than one residual class
mean_model_init.slv	Solver option file to initialize the mean model
mean_model.slvM	Solver option file for the mean model

#### Files for variance model

hvdata.dir	Instruction file for mix99hv (see section <a href="#">10.3.2</a> )
B1/variance_model.[clm mix]	Model definition for the variance model (see section <a href="#">10.4</a> )
B1/variance_model.slvV	Solver option file to variance model
B1/variance_model.var	Variance components for the variance model
*B1/HVbase_ResVar	Standardization variances for traits
*B1/HVbase_ResVarCLASS	Optional: Ratios of standardization variances between different residual classes

#### Additional files for standardization of adjustment factors

HVbaseclasses	Standardization base (see section <a href="#">10.6.1</a> )
*HVbase_ResVarLEVEL	Optional: Control standardization variance estimation for traits

\*Name can not be changed

Solving multiplicative mixed effect model requires several steps. To help users we provide an example script [runMMM](#) located in `examples/heterogeneous_variance` directory that can be used as a starting point when solving larger models with HV correction. Workflow of running MMM is presented in the following table. Input files are the same as in previous table.

### Workflow for running MMM

#### In mean model directory

- |   |                      |                                       |   |
|---|----------------------|---------------------------------------|---|
| 1 | <code>mix99i</code>  | <code>mean_model.clim</code>          | Initialize mean model   |
| 2 | <code>imake99</code> |                                       | Additional pre-processing program mean model                                    |
| 3 | <code>mix99p</code>  | <code>&lt; mean_model_init.svl</code> | Run couple of iterations of mean model to get initial values for variance model |
| 4 | <code>mix99hv</code> | <code>&lt; hvdata.dir</code>          | Create data for variance model  |

#### In B1 directory

- |   |                      |                                      |  |
|---|----------------------|--------------------------------------|--|
| 5 | <code>mix99i</code>  | <code>variance_model.clim</code>     | Initialize variance model                            |
| 6 | <code>imake99</code> |                                      | Additional pre-processing program for variance model |
| 7 | <code>mix99p</code>  | <code>&lt; variance_model.slv</code> | Solve variance model                                 |

#### In mean model directory

- |   |                     |                                  |  |
|---|---------------------|----------------------------------|--|
| 8 | <code>mix99p</code> | <code>&lt; mean_model.slv</code> | Solve MMM. Mean model solver calls script <code>solve_HVmodel</code> . That runs step 7 in each cycle and updates lambda values. |
|---|---------------------|----------------------------------|--|

In addition to files created by standard MiX99 solver the HV solving process creates files to exchange information between mean and variance model and provide information to user. The following table lists the most important files. Filenames containing standard output from MiX99 software follows the script [runMMM](#) shipped with MiX99 package.

#### Files created by MiX99hv

- |                            |                                  |
|----------------------------|----------------------------------|
| <code>tmpHV/HV.data</code> | Data for variance model          |
| <code>tmpHV/HV.pedi</code> | Pedigree file for variance model |

#### Optional files created by mean model solver

- |                             |   |
|-----------------------------|---|
| <code>ARsiwi.data(i)</code> | Heterogeneity observations and weights for variance model. Used when estimating VC for variance model. See section (10.5.1) |
| <code>AR.pedi.reml</code>   | Information about AR correlation structure  |

#### Log files created by [runMMM](#)

- |                          |   |
|--------------------------|---|
| <code>Mi.log</code>      | Mean model initialization ( <code>mix99i</code> ) |
| <code>imake99.log</code> | Mean model <code>imake99</code>                   |

Ma.log	Log for first iterations on mean model ( <a href="#">mix99p</a> )
HVd.log	Log from variance model data creation ( <a href="#">mix99hv</a> )
B1/Vi.log	Variance model initialization ( <a href="#">mix99i</a> )
B1/imake99.log	Variance model <a href="#">imake99</a>
B1/Vs.log	Variance model solving. All cycles. ( <a href="#">mix99p</a> )
Ms.log	Log for solving multiple mixed model

**Log files created by MiX99**

CYC.log	Output from <a href="#">solve_HVmodel</a> . (see section <a href="#">10.10.3</a> )
Lambda.log	Lambda values. (see section <a href="#">10.10.4</a> )

## 10.9 Example

Accounting for [heterogeneous variance](#) in a small test-day model. This example is also shipped with MiX99 package and can be run with script [runMMM](#). The script carefully verifies that all the steps are performed without errors.

[Mean model](#) is a random regression model. [Variance model](#) includes fixed month strata and autocorrelation structure is applied between consecutive years within herd.

**Instruction file for mean model ([mean\\_model.clm](#)):**

```

1 TITLE Heterogeneous variance adjustment by Meuwissen approach: a demonstration
2
3 DATAFILE mean_model.dat
4 INTEGER Month Animal Herd HerdYear Year
5 REAL Covar_1 Covar_2 Milk
6 DATASORT BLOCK=Herd PEDIGREECODE=Animal
7
8 PEDFILE mean_model.ped
9 PEDIGREE G am
10
11 PARFILE mean_model.var
12
13 TMPDIR tmpMiX
14 MISSING 0.0
15
16 MODEL
17 Milk = Covar_1 Covar_2 Month HerdYear G( 1 Covar_1 Covar_2 | Animal )
18
19 WITHINBLOCKORDER G HerdYear
20
21 PRECON d d b
22 PARALLEL 2 1

```

**Instruction file for [mix99hv hvdata.dir](#) :**

```

1 # Instruction file for mix99hv
2 # This is needed to allow mix99hv to create a data and pedigree file
3 # for the variance model
4 # -----
5 #
6 # Name of the data file
7 mean_model.dat
8 # Number of integer columns; type of file (f/u)
9 5 f
10 # Column with the trait group code
11 0
12 # Column with the block variable for the auto regress. proc.

```

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

```
13 # (HERD)
14 3
15 # Heterogeneity Model:
16 # Fixed across block strata; random within block strata
17 # (Month) (Year within Herd)
18 1 5
19 # Create pedigree file for REML-analysis? (y/n)
20 n
21 # Standardisation of multiplicative adjustment factors? (y/n)
22 n
23 # Name of file with the class codes of the base
24 # ID.Base.Classes
25 # Approximation of rank across traits (y/n)
26 y
27 # Random HY effect: Combining of second and third lactation in the variance model
28 1
29 # Directory for the temporary files
30 ./tmpHV
```

### **Instruction file for the variance model (variance\_model.clm):**

```
1 TITLE VARIANCE MODEL
2
3 DATAFILE BINARY ../tmpHV/HV.data
4 INTEGER BLCK HERDxYR TRGRP MONTH
5 REAL HET_OBS WGHT
6 MISSING -8192.0
7 TRAITGROUP TRGRP
8
9 DATASORT BLOCK=BLCK PEDIGREECODE=HERDxYR
10
11 PEDFILE ../tmpHV/HV.pedi
12 PEDIGREE HERDxYR ar
13
14 PARFILE variance_model.var
15 AR 0.7
16
17 MODEL
18 HET_OBS(1) = MONTH HERDxYR ! WEIGHT=WGHT
19
20 PRECON d d
21 PARALLEL 2 0
22 WITHINBLOCKORDER HERDxYR
23 TMPDIR ../tmpMiX/B1
```

### **File with standardization variances HVbase\_ResVar:**

```
1 1.089320
```

### **MiX99 solver option file mean\_model\_init.slvI:**

```
1 # RAM RAM demand: H=high, M=medium, L=low
2 H
3 # STOP Maximum_number_of_iterations, Stopping_criteria (CR)
4 20 1.0e-7
5 # RESID Calculate residuals? (Y/N/H)
6 N
7 # VALID Information for model validation
8 N
9 # VAROPT Adjust for heterogeneous variance (N, E, S, C, G)
10 S
11 # SOLTYP Type of solution files? (N,Y,A,H)
12 N
```

**MiX99 solver option file *variance\_model.slvV*:**

```

1 # RAM      RAM demand: H=high, M=medium, L=low
2           H
3 # STOP     Maximum_number_of_iterations, Stopping_criteria (CR)
4           25      1.0e-7
5 # RESID    Calculate residuals? (Y/N/H)
6           N
7 # VALID    Information for model validation
8           N
9 # VAROPT   Adjust for heterogeneous variance (N, S, C)
10          N
11 # SOLTYP   Type of solution files? (N,Y,A,H)
12          H
    
```

**MiX99 solver option file *mean\_model.slvM*:**

```

1 # RAM      RAM demand: H=high, M=medium, L=low
2           H
3 # STOP     Maximum_number_of_iterations, Stopping_criteria (CR)
4           1000    1.0e-7
5 # RESID    Calculate residuals? (Y/N/H)
6           N
7 # VALID    Information for model validation
8           N
9 # VAROPT   Adjust for heterogeneous variance (N, S, C)
10          C
11          # STOPC Maximum_number_of_cycles, Stopping_criteria for lambdas (CD)
12          80      1.0e-7
13 # SOLTYP   Type of solution files? (N,Y,A,H)
14          Y
    
```

**File with variance components for the variance model *variance\_model.var*:**

```

1  1  1  1  0.078485
2  2  1  1  0.590860
    
```

## 10.10 Output files

There are several sources to follow the progress of the [heterogeneous variance adjustment](#) process: information written to [standard output](#), [HVd.log](#), [CYC.log](#) and [Lambda.log](#).

### 10.10.1 Mi.log and Ms.log

Standard output from [mix99i](#) and [mix99p](#) are written to the files [I.log](#) and [S.log](#) for the *mean model*, respectively, and for the *variance model* it is written to [Vi.log](#), [Vs.log](#), respectively. Each cycle, [mix99p](#) output from the *variance model* will be appended to [Vs.log](#).

[Standard output](#) from the main script [runMMM](#) contains general information about the progress of the HV adjustment and is explained in more detail. The output informs about the current stage of calculation: INITIALIZATION, START ADJUSTMENT CYCLES, CYCLE END, FINAL ITERATION ON MEAN MODEL.

During each cycle the following information is provided (for a simple single trait model):

```

1 .
2 Solve Variance-Model
    
```

## TECHNICAL REFERENCE GUIDE FOR MIX99 SOLVER

```
3   Last HV cycle:                2
4   Lambda criterion CD   =   4.59369973910834D-006
8.85770073643941D-004
5                                     # convergence of the adjustment factors
6                                     # for lambda values of first and second
7                                     # effect in the variance model
8   rhs' M^-1 * rhs   =   318.854161366479
9   -----
10  8   0.6804E-02   0.000   0.000   0.000
11  9   0.3163E-02   0.000   0.000   0.000
12 10  0.3698E-02   0.000   0.000   0.000
13 11  0.3698E-02   0.000   0.000   0.000
14                                     # iteration on mean model
15 Re:   56.1916   # Standardization variance
16 Residual class:  1
17 NStrata          22.0000   # number of strata for each trait
18 zHatMean         0.3248   # average absolute value of z(z is minimized)
19 wHatMean         2.4492   # average weight associate with z's
20 .
```

### 10.10.2 HVd.log

This output provides information about the data and model structure for the [variance model](#).

For instance:

```
1   Number of Blocks in the Data:          57949
2   Largest Class in Blocks found:         21
3   Largest Class in Fixed Strata:        675
4   Shift variable:                       100
5   Largest Random Stratum Code:         5794921
```

For routine evaluations it might give a large amount of warnings of the following form:

```
1 Block without si and wi values: renum.block code= 3771
2 Current number of blocks: 3713
```

This means that the block (herd) has not enough information to calculate residual variances for the strata in the block. For instance if the strata are herd test-days and there is only one cow in a herd.

For such a block a second warning will be written:

```
1 Warning!!! Block without HV-obs. in AR classes.
2 Block= 3713 ignored.
```

For such a case the adjustment factors will be set to 1.0. If the number of such block is rather large one might consider a different [variance model](#).

### 10.10.3 CYC.log

Every cycle `mix99p` calls the script `solve_HVmodel`. Output from this script as well as a sample of adjustment factors it written to `CYC.log`.

During each cycle the following information is provided (for a simple single trait model):

## TECHNICAL REFERENCE GUIDE FOR MIX99 SOLVER

```
1 .
2 Tue Apr 20 11:11:23 EEST 2004
3 Variance_model-iterations: 12 Convergence crit (Cr): 0.3716E-07
4 Lambda convergence (Cd):5.25599751543677D-006 0.00000000000000D+000
5 Beta convergence (Cr): 2.21850223850421D-002
6 Acceleration = 16.0800328372335 2 Used = 1.25000000000000
7 Lambda values for first 30 fixed strata:
8 -----
9 Code,      Trait 1, 2, 3, ...
10      1  0.9130
11      2  0.9416
12      3  0.9674
13      4  1.0524
14      5  1.1232
15
16 Lambda values for random strata:
17 -----
18 Block, AR_class, Traits: 1, 2, 3, ...
19
20      1  1  1.0152
21      1  2  1.0140
22      2  1  1.0173
23      2  2  1.0142
24      3  1  0.9769
25      3  2  0.9849
26      4  1  0.9911
27      4  2  0.9874
28 .
```

The sample of adjustment factors allows visual inspection (by plotting the adjustment factor of one class) of convergence.

### 10.10.4 Lambda.log

This file is created every cycle by the master process of `mix99p`. On distributed memory platforms the file will be written to the directory of the master node. `Lambda.log` contains the lambda values of all strata of the first effect and a sample of lambda values of strata of the second effect in the `variance model`. It also provides information about the standardization of variances. From the `Lambda.log` file one can check whether the lambda values are within a reasonable range. Normally between 0.6 and 1.9. Some values might be smaller or larger. In case a large amount of values is 0.37 ( $\exp(-1)$ ) or 2.72 ( $\exp(1)$ ) something might go wrong. The latter values are the maximum allowed deviations of adjustment factors from 1.0.

## 11 Acknowledgement

The Biometrical Genetics Team at Natural Resources Institute Finland is kindly acknowledged for the valuable suggestions, comments and for being the beta tester of new MiX99 versions.

## 12 References

- Gilmour, A. R. and Thompson, Robin (1998). "Reformulated generalised linear (mixed) model aids multiple trait genetic evaluation with polychotomous calving ease". In: *Proc. 6<sup>th</sup> World Congr. Genet. Appl. Livest. Prod.* Vol. 20, pp. 613–616 (cit. on p. 36).
- Harris, B. and Johnson, D. (1998). "Approximate Reliability of Genetic Evaluations Under an Animal Model". In: *J. Dairy Sci.* 81.10, pp. 2723–2728. DOI: [10.3168/jds.S0022-0302\(98\)75829-1](https://doi.org/10.3168/jds.S0022-0302(98)75829-1) (cit. on p. 30).
- Hesterberg, T. (2005). "Staggered Aitken Acceleraton for EM". In: *Proc. of the American Stat. Assoc.* Minneapolis, Minnesota, USA, 2101—2110. URL: <http://home.comcast.net/~timhesterberg/articles/JSM05-accelerateEM.pdf> (cit. on p. 12).
- Hoeschele, I., Tier, B., and Graser, H. U. (1995). "Multiple-trait genetic evaluation for one polychotomous trait and several continuous traits with missing data and unequal models". In: *J. Anim. Sci.* 73.6, pp. 1609–1627. URL: <http://www.journalofanimalscience.org/content/73/6/1609> (cit. on p. 36).
- Jamrozik, J., Schaeffer, L. R., and Jansen, G. B. (2000). "Approximate accuracies of prediction from random regression models". In: *Livest. Prod. Sci.* 66.1, pp. 85–92. DOI: [10.1016/S0301-6226\(00\)00158-5](https://doi.org/10.1016/S0301-6226(00)00158-5) (cit. on p. 20).
- Janss, L. L. G. and Foulley, J. L. (1993). "Bivariate analysis for one continuous and one threshold dichotomous trait with unequal design matrices and an application to birth weight and calving difficulty". In: *Livest. Prod. Sci.* 33.3–4, pp. 183–198. DOI: [10.1016/0301-6226\(93\)90001-X](https://doi.org/10.1016/0301-6226(93)90001-X) (cit. on p. 36).
- Lidauer, M. and Strandén, I. (1998). "Experience on using parallel computing to solve large test-day models". In: *Proc. 49<sup>th</sup> Ann. Meeting EAAP.* 4. Warsaw, Poland, p. 46 (cit. on p. 1).
- Lidauer, M. and Strandén, I. (1999). "Fast and flexible program for genetic evaluation in dairy cattle". In: *INTERBULL Bulletin.* 20. Tuusula, Finland, pp. 20–25. URL: <https://journal.interbull.org/index.php/ib/article/view/468/466> (cit. on pp. 1, 14).
- Lidauer, M., Strandén, I., Mäntysaari, E. A., Pösö, J., and Kettunen, A. (1999). "Solving large test-day models by iteration on data and preconditioned conjugate gradient". In: *J. Dairy Sci.* 82.12, pp. 2788–2796. DOI: [10.3168/jds.S0022-0302\(99\)75536-0](https://doi.org/10.3168/jds.S0022-0302(99)75536-0) (cit. on pp. 1, 2).
- Lidauer, M., Emmerling, R., and Mäntysaari, E. A. (2008). "Multiplicative random regression model for heterogeneou variance adjustment in genetic evaluation for milk yield in Simmental". In: *J. Anim. Breed. Genet.* 125.3, pp. 147–159. DOI: [10.1111/j.1439-0388.2008.00728.x](https://doi.org/10.1111/j.1439-0388.2008.00728.x) (cit. on p. 48).
- Lidauer, M., Matilainen, K., Mäntysaari, E. A., Pitkänen, T., Taskinen, M., and Strandén, I. (2015). *Technical reference guide for MiX99 pre-processor.* Release VIII/2015. Natural Resources Institute Finland (Luke) (cit. on pp. 1, 3, 4, 9, 11, 14, 17, 18, 33, 37, 39, 40, 42, 59).

- Matilainen, K., Mäntysaari, E. A., Lidauer, M., Strandén, I., and Thompson, R (2012). "Employing a Monte Carlo algorithm in expectation maximization restricted maximum likelihood estimation of the linear mixed model". In: *J. Anim. Breed. Genet.* 129.6, pp. 457–468. DOI: [10.1111/j.1439-0388.2012.01000.x](https://doi.org/10.1111/j.1439-0388.2012.01000.x) (cit. on p. 40).
- Matilainen, K., Mäntysaari, E. A., Lidauer, M., Strandén, I., and Thompson, R (2013). "Employing a Monte Carlo algorithm in Newton-type methods for restricted maximum likelihood estimation of genetic parameters". In: *PLoS ONE* 8.12. e80821. DOI: [10.1371/journal.pone.0080821](https://doi.org/10.1371/journal.pone.0080821) (cit. on p. 42).
- Meuwissen, T. H. E., De Jong, G., and Engel, B. (1996). "Joint estimation of breeding values and heterogeneous variances of large data files". In: *J. Dairy Sci.* 79.2, pp. 310–316. DOI: [10.3168/jds.S0022-0302\(96\)76365-8](https://doi.org/10.3168/jds.S0022-0302(96)76365-8) (cit. on pp. 11, 48, 49, 55, 58).
- MiX99 Development Team (2015). *MiX99: A software package for solving large mixed model equations*. Release VIII/2015. Natural Resources Institute Finland (Luke). Jokioinen, Finland. URL: <http://www.luke.fi/mix99> (cit. on p. ii).
- Misztal, I. and Wiggans, G. R. (1988). "Approximation of prediction error variance in large-scale animal models". In: *J. Dairy Sci.* 71, Supplement 2.0, pp. 27–32. DOI: [10.1016/S0022-0302\(88\)79976-2](https://doi.org/10.1016/S0022-0302(88)79976-2) (cit. on p. 20).
- Mrode, R. A. and Swanson, G. J. T. (2004). "Calculating cow and daughter yield deviations and partitioning of genetic evaluations under a random regression model". In: *Livest. Prod. Sci.* 86.1–3, pp. 253–260. DOI: [10.1016/j.livprodsci.2003.09.001](https://doi.org/10.1016/j.livprodsci.2003.09.001) (cit. on pp. 8, 32).
- Shewchuk, J. R. (1994). *An introduction to the conjugate gradient method without the agonizing pain*. URL: <http://www.eletrica.ufpr.br/artuzi/te804/arquivos/cg.pdf> (cit. on p. 2).
- Strandén, I. (1999). "Parallel benefits in test-day evaluations". In: *INTERBULL Bulletin*. 20. Tuusula, Finland, pp. 26–32. URL: <https://journal.interbull.org/index.php/ib/article/view/469/467> (cit. on p. 1).
- Strandén, I. (2015). *Command Language Interface for MiX99*. Release VIII/2015. Natural Resources Institute Finland (Luke) (cit. on pp. 1, 4, 9).
- Strandén, I. and Lidauer, M. (1999). "Solving large mixed linear models using preconditioned conjugate gradient iteration". In: *J. Dairy Sci.* 82.12, pp. 2779–2787. DOI: [10.3168/jds.S0022-0302\(99\)75535-9](https://doi.org/10.3168/jds.S0022-0302(99)75535-9) (cit. on pp. 1, 3).
- Strandén, I., Lidauer, M., Mäntysaari, E. A., and Pösö, J. (2000). "Calculation of Interbull weighting factors for the Finnish test day model". In: *INTERBULL Bulletin*. 26. Verden, Germany, pp. 78–79. URL: <https://journal.interbull.org/index.php/ib/article/view/366/366> (cit. on p. 20).
- Tier, B. and Meyer, K. (2004). "Approximating prediction error covariances among additive genetic effects within animals in multiple-trait and random regression models". In: *J. Anim. Breed. Genet.* 121.2, pp. 77–89. DOI: [10.1111/j.1439-0388.2003.00444.x](https://doi.org/10.1111/j.1439-0388.2003.00444.x) (cit. on p. 20).
- VanRaden, P. M. and Wiggans, G. R. (1991). "Derivation, Calculation, and Use of National Animal Model Information". In: *J. Dairy Sci.* 74.8, pp. 2737–2746. DOI: [10.3168/jds.S0022-0302\(91\)78453-1](https://doi.org/10.3168/jds.S0022-0302(91)78453-1) (cit. on p. 32).
- Wade, K. M. and Quaas, R. L. (1993). "Solutions to a system of equations involving a first-order autoregressive process". In: *J. Dairy Sci.* 76.10, pp. 3026–3032. DOI: [10.3168/jds.S0022-0302\(93\)77642-0](https://doi.org/10.3168/jds.S0022-0302(93)77642-0) (cit. on p. 51).

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

- Vuori, K., Strandén, I., Lidauer, M., and Mäntysaari, E. A. (2006a). "MiX99 – Effective solver for large and complex linear mixed models". In: *Proc. 8<sup>th</sup> World Congr. Genet. Appl. Livest. Prod.* Belo Horizonte, MiG, Brazil, pp. 27–33 (cit. on p. 37).
- Vuori, K., Strandén, I., Sevón-Aimonen, M.-L., and Mäntysaari, E. A. (2006b). "Estimation of non-linear growth models by linearization: a simulation study using a Gompertz function". In: *Genet. Sel. Evol.* 38, pp. 343–358. DOI: [10.1186/1297-9686-38-4-343](https://doi.org/10.1186/1297-9686-38-4-343) (cit. on p. 37).

## Index

### Index entry styles:

- normal index entry
- `shell commands`
- `MiX99 input commands`
- `CLIM input commands`
- `file names`

### Page numbers:

- primary definition: [71](#)
- also referred: [71](#)
-  see example on page

-99999, [38](#)

-8192.0, [8](#), [8](#), [18](#), [54](#), [56](#)

`ACCani`, [29](#)

AccurType (ApaX), [22](#), [30](#), [31](#)

across block strata, [50](#), [52](#)

ADJUST, [11](#), [11](#)

Aitken acceleration, [12](#)

`am`

 [63](#)

`am`, [54](#), [55](#)

 [27](#), [34](#)

`apax99`, [1](#), [20](#), [20–22](#), [26](#), [29](#), [30](#)

`apax99p`, [1](#), [20](#), [20](#), [21](#), [26](#), [30](#)

APPROX (mix99hv), [52](#), [53](#)

`AR`

 [57](#), [64](#)

`ar`

 [57](#), [64](#)

`ar`, [54](#), [55](#), [55](#)

`AR.block`, [53](#)

`AR.pedi.reml`, [52](#), [57](#), [62](#)

ARFILE (mix99hv), [52](#), [57](#)

`ARsiwi.data(i)`, [8](#), [53](#), [57](#), [62](#)

autoregressive model, [54](#), [55](#)

`B1`, [60](#), [60](#)

for temporary files, [56](#), [60](#)

BASEFILE (mix99hv), [52](#), [59](#)

`BINARY`

 [56](#), [64](#)

`BLOCK`

 [57](#), [63](#), [64](#)

`BR2.dat`, [26](#)

`BR2.f90`, [20](#), [26](#)

`CA`, [7](#), [7](#), [14](#), [16](#)

categorical variable, [36](#)

`CD`, [7](#), [7](#), [14](#), [16](#)

`CG`, conjugate gradient, [2](#)

`cl`

 [27](#), [34](#), [45](#)

COMBINE (HV var), [55](#)

COMMONBLOCKS (HV var), [56](#)

conjugate gradient method, [2](#)

convergence indicator, [7](#), [10](#), [12](#), [13](#),  
[15](#), [42](#)

`CA`, [7](#)

`CD`, [7](#)

`CR`, [7](#)

covariable file, [23](#), [37](#)

covariable table, [23](#), [38](#)

covariances of REML estimates, [43](#)

CovarInfo (ApaX), [23](#)

`CR`, [7](#), [14](#), [16](#)

`CYC.log`, [60](#), [65](#), [66](#)

`DATAFILE`

 [45](#), [56](#), [63](#), [64](#)

DATAFILE (HV var), [56](#)

DATAFILE (mix99hv), [51](#)

`DATASORT`

 [56](#), [63](#), [64](#)

daughter yield deviation, [8](#), [10](#), [17](#), [32](#),  
[33](#)

Deregression, [9](#)

`d1amch.f90`, [4](#)

DYD, daughter yield deviation, [8](#), [10](#),  
[32](#), [32](#), [33](#)

EDC, effective daughter contribution,  
[26](#), [26](#)

effective daughter contribution, [26](#)

effective record contributions, [30](#)

`eHat.data(i)`, [7](#), [18](#)

EM REML, [40](#)

EM, Expectation Maximization

## TECHNICAL REFERENCE GUIDE FOR MiX99 SOLVER

- for estimation of variance components, [40](#)
- for Threshold-model, [36](#)
- ERC, [30](#)
- estimation of variance components, [7](#), [10](#), [40](#), [41](#)
- exa99, [1](#), [29](#), [29](#)
- FACTOR, [9](#), [9](#), [33](#)
- first order autoregressive process, [50](#), [51](#), [52](#), [54](#)
- fixed variance components, [10](#), [41](#)
- FIXRAN (HV var), [55](#)
- generating observations, [8](#)
- genomic BLUP, [20](#)
- Gompertz-model, [12](#), [36](#), [37](#), [40](#)
- H2calc (ApaX), [24](#)
- Half-Chebyshev, [12](#)
- heterogeneous variance, [1](#), [8](#), [15](#), [21](#), [48](#), [48](#), [50](#), [60](#), [63](#)
- heterogeneous variance adjustment, [6](#), [10](#), [11](#), [12](#), [14](#), [65](#)
- heterogeneous\_variance, [60](#)
- Hetlog, [53](#)
- HV, heterogeneous variance, [48](#)
- HV.data, [53](#), [53](#), [55–57](#), [62](#)
- HV.info(i), [53](#), [53](#)
- HV.pedi, [53](#), [54](#), [54](#), [56](#), [57](#), [62](#)
- HVbase\_ResVar, [52](#), [58](#), [59](#), [59](#), [61](#), [64](#)
- HVbase\_ResVarCLASS, [59](#), [61](#)
- HVbase\_ResVarLEVEL, [59](#), [61](#)
- HVd.log, [66](#)
- I.log, [65](#)
- ID.Base, [58](#), [58](#)
- IDD, [8](#), [10](#), [32](#)
- IDD.data(i), [8](#), [18](#)
- imake4apax, [21](#)
- imake99, [4](#), [4](#), [5](#), [62](#), [63](#)
- Index.bin, [4](#)
- individual daughter deviation, [8](#), [10](#), [18](#), [32](#)
- information matrix, [43](#)
- instruction file
  - ApaX, [21](#), [26](#), [30](#)
  - CLIM command file, [4](#), [36](#), [40](#), [45](#)
  - Exa, [29](#)
  - HV var, [54](#), [54](#)
  - mix99hv, [51](#), [55–57](#), [59](#), [60](#)
  - preprocessor directive file, [4](#), [4](#), [6](#), [27](#), [36](#), [37](#), [40](#), [51](#)
  - solver option file, [4](#), [6](#), [6](#), [42](#), [45](#), [57](#)
- INT-VAR (HV var), [55](#)
- INTEGER
  -  [45](#), [56](#), [63](#), [64](#)
- IOD, iteration on data, [2](#)
- iteration on data, [1](#), [1](#), [2](#), [4](#)
- iterative method, [2](#)
  - convergence indicator, [7](#)
  - determining convergence, [13](#)
  - interrupting, [15](#)
  - maximum number of iterations, [7](#)
  - nested iterations, [36](#)
  - restarting, [17](#)
  - stopping criterion, [7](#)
- JFilter (ApaX), [24](#), [24](#), [31](#)
- JFilter (Exa), [29](#)
- Lambda.data(i), [53](#)
- Lambda.log, [65](#), [67](#), [67](#)
- ls, [55](#)
- LS-model, [17](#), [50](#), [54–56](#)
- MAS BLUP, [20](#)
- maximum number of iterations, [7](#)
- MaxNonZ (ApaX), [23](#), [31](#)
- MC, Monte Carlo, [40](#)
- MC EM REML, [10](#), [40](#), [41](#), [42](#)
- mean model, [15](#), [48](#), [48–60](#), [63](#)
- Mean\_model.slvM, [57](#), [60](#), [60](#)
- Mean\_model\_init.slvI, [60](#)
- MERGE2 (mix99hv), [53](#), [55](#)
- MISSING
  -  [56](#), [63](#), [64](#)
- missing covariable, [38](#)
- missing observation, [38](#)
  - heterogeneity observation, [56](#)
- missing trait, [36](#), [37](#)
- missing value, [8](#), [8](#), [18](#), [54](#)
- MISSVA (HV var), [56](#)
- MiX99.lst, [5](#), [11](#)
- MiX99\_DIR.DIR, [40](#), [40](#), [41](#), [45](#)
- mix99hv, [11](#), [50](#), [51](#), [51](#), [53–60](#), [62](#), [63](#)

- `mix99i`, [1](#), [4](#), [4](#), [5](#), [8](#), [11](#), [17](#), [18](#),  
[21–23](#), [29](#), [38](#), [40](#), [41](#), [45](#), [53](#),  
[62](#), [63](#), [65](#)
- `mix99p`, [1](#), [4](#), [4–6](#), [8](#), [11–13](#), [17](#), [18](#),  
[21](#), [50](#), [53](#), [58–63](#), [65–67](#)
- MIX99PATH, [11](#)
- `mix99s`, [1](#), [4](#), [4–8](#), [10](#), [11](#), [13](#), [17](#), [18](#),  
[21](#), [38](#), [40–42](#), [45](#)
- `MiXtoolmerge.f90`, [19](#)
- `MiXtoolms.f90`, [19](#)
- `MiXtools`, [18](#), [19](#)
- MMM, multiplicative mixed model, [48](#),  
[49](#)
- MODEL  
    ☞ [45](#), [56](#), [57](#), [63](#), [64](#)
- MODEL (HV var), [55](#)
- model validation, [18](#), [32](#)
- MODVAR (mix99hv), [52](#)
- Monte Carlo, [40](#)
- multiple residual variance matrices, [21](#),  
[42–44](#), [59](#)
- multiplicative mixed model, [11](#), [14](#), [48](#),  
[48](#), [57](#), [60](#)
- mxntra, [8](#), [18](#)
- Newton-Raphson algorithm, [36](#)
- non-linear models, [36](#), [48](#)
- number of data samples, [10](#), [41](#), [42](#)
- NumBVs (ApaX), [23](#), [24](#), [31](#)
- Opzero (Exa), [29](#), [29](#)
- OriginalDir (ApaX), [23](#), [30](#)
- `OutFile`, [26](#)
- PARALLEL  
    ☞ [57](#), [63](#), [64](#)
- PARALLEL (HV var), [56](#), [60](#)
- parallel computing, [1](#), [3](#), [4](#), [4](#), [5](#), [7](#), [15](#),  
[18](#), [20–23](#), [48](#)  
    `apax99p`, [20](#)  
    `mix99p`, [4](#)
- PARFILE  
    ☞ [45](#), [57](#), [63](#), [64](#)
- `parfile`, [43](#), [44](#), [44](#)
- PARFILE (HV var), [56](#)
- PCG, preconditioned conjugate  
    gradient, [2](#), [2](#), [4](#), [7](#), [36](#)
- PEDFILE  
    ☞ [45](#), [57](#), [63](#), [64](#)
- PEDFILE (HV var), [56](#)
- PEDIGREE  
    ☞ [45](#), [57](#), [63](#), [64](#)
- PEDIGREE (HV var), [55](#), [55](#)
- PEDIGREECODE  
    ☞ [57](#), [63](#), [64](#)
- `PEV.bin`, [22](#), [22](#)
- `PEVani`, [26](#), [26](#), [31](#)
- `PEVrnn`, [29](#)
- PRECON  
    ☞ [57](#), [63](#), [64](#)
- PRECON (HV var), [56](#)
- preconditioned conjugate gradient  
    method, [1](#), [2](#)
- preconditioning, [2](#), [13–16](#), [21](#), [38](#), [41](#)  
    block diagonal, [15](#), [15](#), [33](#)  
    diagonal, [15](#), [15](#)  
    full block, [15](#)  
    updating, [11](#), [41](#)
- predicted observations, [8](#), [18](#)
- RAM, [6](#)
- RANDOM (HV var), [55](#)
- random\_seed, [10](#)
- RANSOLFILE (HV var), [56](#)
- REAL  
    ☞ [45](#), [56](#), [63](#), [64](#)
- REAL-VAR (HV var), [55](#)
- REGRESS (HV var), [55](#)
- RELATIONSHIPS (HV var), [55](#)
- reliability  
    approximation, [1](#), [20](#)  
    exact, [1](#), [29](#)  
    reversed, approximation, [30](#)
- REML, [10](#), [40](#), [41](#), [42](#), [44](#)
- `REMLlog`, [43](#), [44](#), [44](#)
- `resfile`, [44](#)
- RESID, [7](#), [18](#), [57](#)
- residuals, [6–8](#), [9](#), [18](#)
- restart iteration, [17](#)
- reversed reliability approximation, [22](#),  
[30](#)
- RHO (HV var), [55](#)
- runMMM, [53](#), [60](#), [61–63](#), [65](#)
- `S.log`, [65](#)
- SCALE (HV var), [56](#)
- SEED, [9](#), [10](#)
- `SEfnn`, [29](#)

- SEfix, [29](#)
- SEreg, [29](#)
- SETLOSS (mix99hv), [53](#)
- sHat.data(i), [8](#), [18](#)
- simulating observations, [8](#)
- SireFile, [26](#)
- SiWi.data(i), [11](#)
- sm
  -  [45](#)
- sm
  -  [45](#)
- Sol\_mn, [17](#)
- Solani, [17](#), [26](#), [33](#)
- SolaniB, [12](#)
- Solcommon, [17](#)
- Soldyd, [8](#), [17](#), [33](#), [34](#)
- Solfnn, [17](#)
- Solfix, [17](#), [37](#)
- SolfixB, [12](#)
- Solold, [18](#)
- Solpriv(i), [17](#)
- Solrnn, [17](#)
- Solreg, [17](#)
- SOLTYP, [12](#), [38](#)
- Solunf, [18](#)
- SOLUNF (HV var), [56](#)
- solve\_HVmodel, [60–63](#), [66](#)
- Solvec, [17](#), [17](#), [18](#)
- SORT\_B (mix99hv), [52](#)
- SORT\_R (HV var), [24](#), [55](#)
- Sparse\_Matrix.DMPz, [23](#)
- STAND (mix99hv), [52](#), [59](#)
- standard errors
  - for fixed effects, [29](#)
  - for variance components, [42](#)
- standard output, [17](#), [33](#), [65](#)
- StartDIM (ApaX), [23](#)
- STOP, [6](#), [7](#), [11](#), [36](#)
- STOP, [15](#), [15](#)
- STOPC, [12](#), [60](#)
- STOPE, [10](#), [41](#), [42](#)
- stopping criterion, [7](#)
- stopping iteration, [15](#)
- sum of selected model factors, [8](#), [18](#)
- threshold-model, [7](#), [36](#), [36](#), [40](#)
- TITLE
  -  [45](#), [56](#), [63](#), [64](#)
- TITLE (HV var), [55](#)
- Tm10.trco(i), [4](#)
- Tm10.trco0, [4](#)
- Tmp4.pedi(i), [4](#)
- Tmp4.pedi0, [4](#)
- Tmp5.clas(i), [4](#)
- Tmp5.clas0, [4](#)
- Tmp6.diab(i), [4](#)
- Tmp6.diab0, [4](#)
- TMPDIR
  -  [63](#), [64](#)
- TMPDIR (HV var), [56](#)
- TMPHV (mix99hv), [53](#), [61](#)
- TRAITGROUP
  -  [56](#), [64](#)
- TRAITS (HV var), [55](#)
- TRGRP (HV var), [55](#)
- TRGRP (mix99hv), [52](#)
- VALID, [8](#), [11](#), [18](#), [32](#), [33](#)
- VAR (HV var), [56](#)
- VAR\_I (mix99hv), [52](#)
- variance model, [11](#), [12](#), [15](#), [48](#), [48–60](#), [63](#), [65–67](#)
- Variance\_model.slvV, [60](#)
- VAROPT, [9](#), [10](#), [10–12](#), [14](#), [41](#), [42](#)
- vceI, [43](#), [44](#)
- vceSE, [43](#), [44](#), [44](#)
- Vi.log, [65](#)
- Vs.log, [65](#), [65](#)
- WEIGHT
  -  [57](#), [64](#)
- Weights (ApaX), [23](#), [24](#)
- within block strata, [50](#), [51](#), [52](#), [58](#)
- WITHINBLOCKORDER
  -  [57](#), [63](#), [64](#)
- WITHINBLOCKORDER (HV var), [55](#)
- work files, [2](#), [4](#), [4](#)
- YD, yield deviation, [8](#), [32](#)
- YD.data(i), [8](#), [18](#)
- yHat.data(i), [8](#), [18](#)
- yield deviation, [6](#), [8](#), [9](#), [18](#), [32](#)
- ySim.data0, [9](#)