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AngelPedTK- An efficient toolkit for comprehensive animal pedigree management

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ABSTRACT

Acquiring an accurate raw pedigree for animal genetic analyses is a challenging task. The sources of errors are mostly personnel or farmers who manage pedigree information. To date, many softwares are found for animal breeding research featuring faster and advanced algorithms for animal data analyses. However, these softwares are deemed incomplete or lack proper functionalities, especially for comprehensive pedigree handling. We, therefore, developed a suit software packages namely **AngelPedTK** (Animal Genetic Evaluation Laboratory Pedigree Toolkit) version 1.0 to support a comprehensive pedigree management and enhance the user-experience while being computation efficient. AngelPedTK is collection of four base modules- *PedCheck* (to check pedigree errors), *PedTrace* (to create a sub-pedigree which contains animals for the analysis from whole pedigree), *PedStack* (to prune pedigree and generate a chronologically ordered pedigree such that parents appear before their progeny), and *PedGetF* (to calculate numerator relationship matrix (NRM), inbreeding coefficient and pedigree completeness index). This toolkit includes both command-line interface and a graphical user interface (GUI). The core modules are written in low-level C language enabling faster data processing. The GUI front end is a wrapper module built on top of the core modules to provide a flexible working environment. Although implementation of GUI, which most available softwares limits, comes at a cost of memory usage or a little processing expense, yet a good balance is maintained due to the deployment of efficient algorithm. We hope that this software will assist a large range of users through user-friendly features and processing comprehensiveness.

Keywords: AngelPedTk, software, pedigree preparation, inbreeding coefficient, pedigree completeness

Introduction

Acquiring an accurate pedigree in animal breeding studies have always been major concerns for animal breeders. Even to date, most of the pedigree records are collected by farmers or agency personnel which makes it difficult to avoid pedigree related errors completely. For this reason, animal breeding researchers have written various computer software packages to perform pedigree correction using basic principles of pedigree formation. Most of those softwares i.e., ASReml (Gilmour et al., 2009), WOMBAT (Mayer, 2007), BLUPF90 (Misztal et al., 2002), PEDIG (Biochard, 2002), CFC (Sargolzaei et al., 2006), and many R packages were mostly designed to perform statistical analysis on pre-processed pedigree. Although some packages offer arrays of functions or features for pedigree processing, those lack user-friendly environment and require some

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level of computing skills. This is because such packages were written mostly for a cleaned pedigree and used sophisticated programming languages i.e., FORTRAN, C or R to obtain higher computation efficiency. Some of them are machine platform (Windows or Linux) dependent too. As a common scenario, some packages might ignore errors through deletion of erroneous records and continue to next steps or even if reports error would be difficult to trace back.

Therefore, we report a pedigree management software package (Animal Genetic Evaluation Laboratory Pedigree Toolkit or ***AngelPedTk***) which is designed to optimize user experiences greatly while ensuring computing efficiency as possible. This toolkit consists of a set of four modules featuring both basic command line interface (CLI) and a graphical user interface (GUI) environment. Basic precompiled modules are invokable through Windows command prompts independently, and run in batch-mode with other programs. However, the GUI interface is a wrapper module over these CLI based core precompiled executables offering many window-based front-end features for a smoother user control over the pedigree management and estimation processes. In other words, the GUI accepts required arguments and processed them through precompiled executables.

Computing Methods

AngelPedTk is a collection of four modules (CLI based executable) written in C programming language. Additionally, this software provides a GUI wrapper for these modules (Figure 1), written under Qt 4.8 software development framework, which creates an easy-to-use and user-friendly pedigree processing environment for users of no prior programming experiences. The core version of this toolkit (command line) are designed with overloading and optional parameters. Although runtime optimization was not our primary objective for simplicity sake, these programs execution are generally faster even with large datasets due to the advantages of low-level C language. We implemented a fairly a large hash-table data structure (max. 1,000,000 buckets) so that moderately larger pedigree datasets could be processed easily. This toolkit also supports larger animal ID (upto 32 alphanumeric characters) for which some widely used pedigree based softwares are limited.

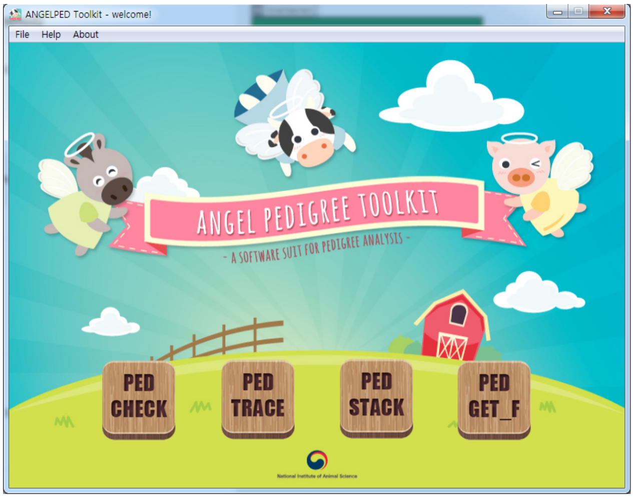

ANGELPED Toolkit - welcome!
File
Help
About
ANGEL PEDIGREE TOOLKIT
- A SOFTWARE SUIT FOR PEDIGREE ANALYSIS -
PED CHECK
PED TRACE
PED STACK
PED GET_F
National Institute of Animal Science

Figure 1. The main fornt-end GUI of AngelPedTk.

Modules And Purposes

Four standalone modules included with this toolkit are designed for specific tasks. The primary functions of each module are summarized as bellow:

1. ***PedCheck*** − a tool for pedigree errors check,
2. ***PedTrace*** − a tool of creating sub-pedigree from a whole pedigree for given animals,
3. ***PedStack*** − a tool for complete pedigree stacking of given animals,
4. ***PedGetF*** − a tool for pedigree sorting (chronological ordering), renumbering, calculation of inbreeding, coefficients, and pedigree completeness index.

Although, we suggest a sequential execution in above listed order to obtain more control on pedigree processing, users can follow any order of executions if required input files are already prepared.

The *PedCheck* Module

Typically, a pedigree file consists of three columns representing animal (progeny ID), sire, and dam, respectively. In practice, several types of pedigree errors could occur, mostly due to human errors. Generally, pedigree records are considered incorrect when an animal ID appears as (I) its own sire and/or dam, (II) a parent differently (sire and dam) between progenies, and iii) like error II except that its own pedigree is also missing. Additionally, duplicated animal records (rows) are often discouraged, even though those might not be errors in true sense. But these duplicated records could be expensive regarding memory and processing time, and thus are avoided as possible. *PedCheck* module searches for such errors and reports accordingly for necessary actions. As of features implemented, it supports both free or fixed format files with single or mixed data field delimiters (Table 1 & 2; Figure 2). By default, missing values are set to zero and all columns values are considered as alphanumeric type unless specified explicitly.

Table 1. Commands and arguments for tools in ANGELPED Toolkit on a windows platform

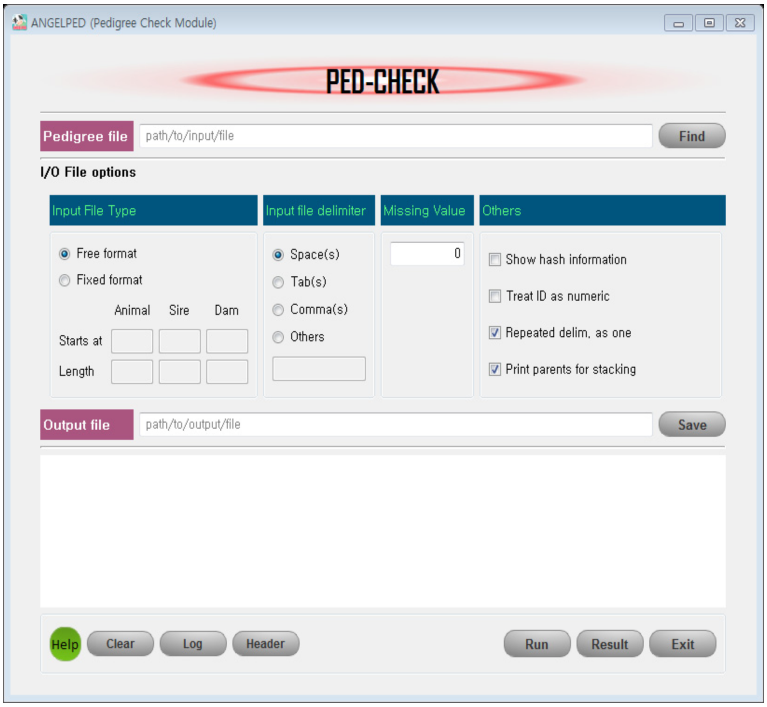
Program	Command line option and argument[1]				
PedCheck	PedCheck.exe	[Option(s)]	<Input_File>	<Output_File>	
PedTrace	PedTrace.exe	[Option(s)]	<Input_File>	<Key_File>	<Output_File>
PedStack	PedStack.exe	[Option(s)]	<Input_File>	<Output_File>	
PedGetF	PedGetF.exe	[Option(s)]	<Input_File>	<Output_File>	

[1]The orders of input, key and output files are important, whereas option sequences are insignificant

Table 2. List of command line arguments for tools in ANGELPED Toolkit[1]

Option association	Tag	PC	PT	PS	PF	Remark
Renumbered pedigree	-c	-	-	-	∨	Prints renumbered IDs in the output file.
Input file delimiter	-d	∨	∨	∨	∨	Single or mixed type (, \t “ ” ‘ ’ .\t‘’); whitespace is set default with -r.
Output file delimiter	-D	-	∨	∨	∨	Single or mixed type (, \t “ ” ‘ ’ .\t‘’); whitespace is set default.
Output error file	-e	-	-	∨	-	Replaces default log (PedStack.err) to filename specified.
Column details	-f	∨	∨	∨	∨	-f [pos] [len]; i.e. -f 1, 5, 6, 5, 11,5.
Generation loop error	-g	-	-	∨	-	Default is 50. Program will detect cycling error at >50 generations.
Hash-table information	-h	∨	∨	∨	∨	Prints detailed hash information only.
Non-traced animal	-i	-	∨	-	-	Print non-traced animal ID in the output file.
Missing value	-m	∨	∨	∨	∨	Default: ‘whitespace’ (with -f), 0 (without -f); i.e. 0, -999.
Type of animal ID	-n	∨	∨	∨	∨	Treat ID as numeric and ignore leading zeros (if any).
Prune founder/PCI	-p	-	-	∨	∨	PS: -p 1 (pedigree pruning); PF: -p (printing PCI upto 5 generations)
Delimiter conversion	-r	∨	∨	∨	∨	Converts repeated delimiters into a single delimiter.
Parent stacking	-s	∨	∨	∨		Print parents to be stacked.
Tabular method	-t	-	-	-	∨	Default: Meuwissen & Luo (1992) algorithm for F calculation.

[1]PC, PedCheck; PT, PedTrace; PS, PedStack; PF, PedGetF; PCI, Pedigree Completeness Index; F, Inbreeding coefficient


ANGELPED (Pedigree Check Module)

Pedigree file: path/to/input/file

I/O File options

Input File Type: ● Free format ○ Fixed format

	Animal	Sire	Dam
Starts at			
Length			

Input file delimiter: ● Space(s) ○ Tab(s) ○ Comma(s) ○ Others

Missing Value: 0

Others:
□ Show hash information
□ Treat ID as numeric
☑ Repeated delim. as one
☑ Print parents for stacking

Output file: path/to/output/file

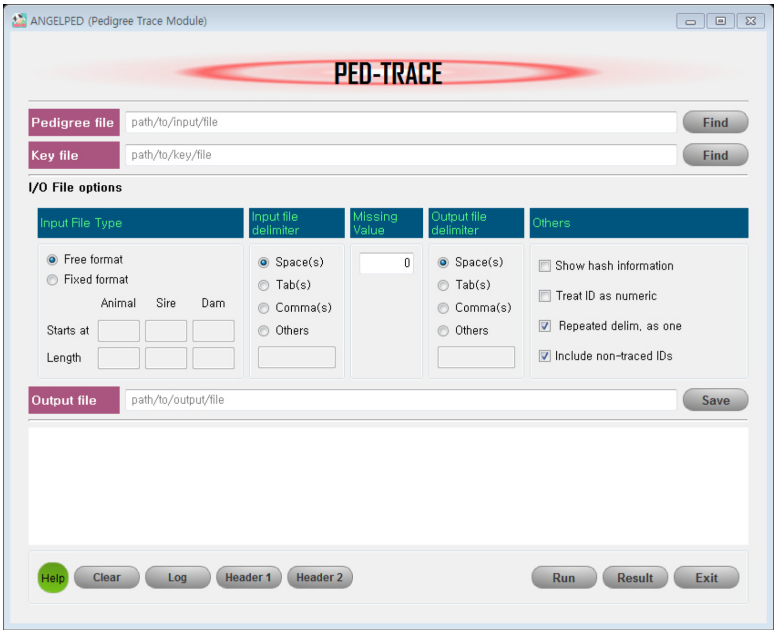
Figure 2. The front-end GUI for *PedCheck* module.

The *PedTrace* Module

In animal genetic study, it is often found that pedigree files are obtained from a source as is, whereas a user may need a desired (reduced) pedigree for animals with phenotypic records only. This module is especially written for searching related pedigrees for such purposes. This program (Table 1 & 2; Figure 3) also shares many similar features as been implemented in *PedCheck* program. Note that a key file with animals listed is a requirement for this module. Non-traced animals can also be included in the output file. This pedigree processing phase is especially important in a sense that those unrelated pedigrees is unable to add extra relationship information to the model with respect to animal phenotypes. Instead, those unrelated pedigrees can increase data processing time significantly.

The *PedStack* Module

This module is written for generating a stacked pedigree structure according to generations. Usually, breeding values are estimated using Henderson's mixed model equation (BLUP; Henderson, 1973), where animal relationships are accounted for capturing additive genetic variations. Calculating numerator relationship matrix (NRM) could be a tedious work if done by hand or even by computers, and therefore, different algorithms emerged over the years to improve computing efficiency. One of the most efficient algorithm is to stack animals according to generations where parents appear before progenies. This calculates relationships sequentially and avoids double counting of animals. Therefore, it reduces NRM creation time very significantly, even with larger pedigrees. However, animal ordering according to generations becomes difficult if birthday records are not kept at all or partial. So, with no dependency on birthdays, *PedStack* module uses an algorithm for ordering pedigrees by generations (Kim et al., 2006). By default, it is set to order animals upto 50 generations under the assumption that circular pedigree errors (progeny becomes ancestor of an ancestor) may occur where animal generation extends beyond 50. The *PedStack* module (Table 1 & 2; Figure 4) also allows pruning of parents in the founder group based on minimum number of progenies. The default value of 1 for pruning indicates that this parent has appeared only once in the progeny generation while its own pedigree is missing. Therefore, this parent will be discarded from or treated as missing in the output pedigree. These default features are easily modifiable too. Note that with prior knowledge of no existing errors in the raw pedigree and with no need for *PedTrace* phase, a user can directly proceed through *PedStack* step to generate a comprehensive stacked pedigree from the raw data.



ANGELPED (Pedigree Trace Module)

PED-TRACE

Pedigree file: path/to/input/file

Key file: path/to/key/file

I/O File options

Input File Type: ● Free format ○ Fixed format

	Animal	Sire	Dam
Starts at			
Length			

Input file delimiter: ● Space(s) ○ Tab(s) ○ Comma(s) ○ Others

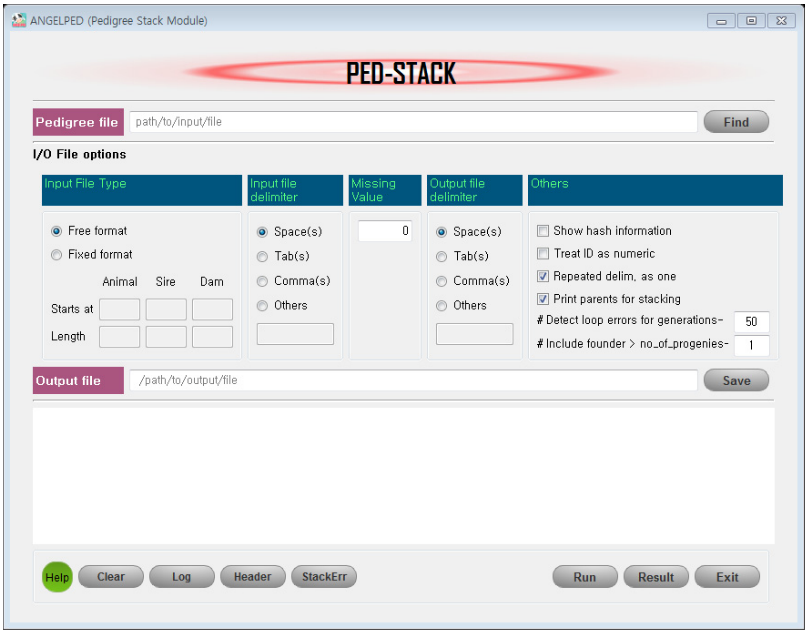
Missing Value: 0

Output file delimiter: ● Space(s) ○ Tab(s) ○ Comma(s) ○ Others

Others:
- □ Show hash information
- □ Treat ID as numeric
- ☑ Repeated delim. as one
- ☑ Include non-traced IDs

Output file: path/to/output/file

Figure 3. The front-end GUI for *PedTrace* module.



ANGELPED (Pedigree Stack Module)

PED-STACK

Pedigree file: path/to/input/file

I/O File options

Input File Type: ● Free format ○ Fixed format

	Animal	Sire	Dam
Starts at			
Length			

Input file delimiter: ● Space(s) ○ Tab(s) ○ Comma(s) ○ Others

Missing Value: 0

Output file delimiter: ● Space(s) ○ Tab(s) ○ Comma(s) ○ Others

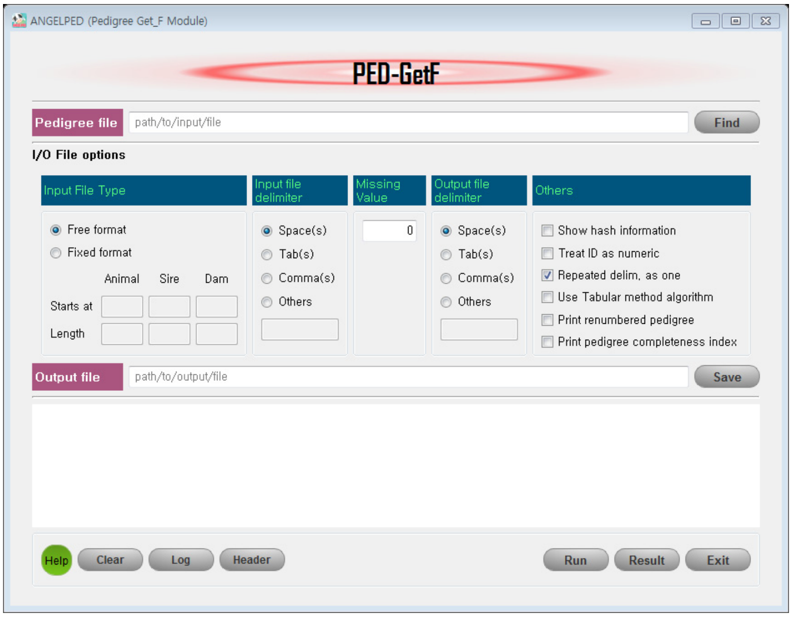
Others:
- □ Show hash information
- □ Treat ID as numeric
- ☑ Repeated delim. as one
- ☑ Print parents for stacking
- # Detect loop errors for generations- 50
- # Include founder > no_of_progenies- 1

Output file: /path/to/output/file

Figure 4. The front-end GUI for *PedStack* module.

The *PedGetF* Module

Animal breeding value estimation is commonly based on mixed-model equation (MME) using Henderson's BLUP method. An essential step to do this is to obtain an inverse of relationship matrix A (additive genetic relationship) for animals. A is a symmetric matrix and its diagonal element for an animal i is equal to 1 + F_i, where F_i is the inbreeding coefficient of animal i (Wright, 1922). Over time clever and elegant but simple rules were coined to build the inverse of A (Henderson, 1976). Advanced concepts such as iteration on data concept (IOD; Schaeffer and Kennedy, 1986) can avoid the need for direct calculation of inbreeding coefficient as well. However, a simple decomposition of relationship matrix is known as A=TDT′ (Thompson, 1977), where T is a lower triangular matrix and D is a diagonal matrix for Mendelian sampling. A detail of this decomposition is found in Mrode (2014). In summary, to obtain an inverse of A, the diagonal element (B_{ii}) of D^{-1} is needed (see NIAS, 2012 for calculating B_{ii}). This module can compute B_{ii} elements. For inbreeding coefficient calculation, we implemented Meuwissen and Luo (1992) algorithm as a default option. However, our observation showed that when the animals in pedigree are highly inbred, the computation of F using tabular method (see details in Tier, 1990) as attributed to Lush by Emik and Terrill (1949, cited by Hudson et al, 1982) deemed more efficient. *PedGetF* (Table 1 & 2; Figure 5) uses a variance covariance matrix (Henderson C.R., 1976) with an optional argument. The pedigree completeness index (PCI, MacCluer et al., 1983) usually provides information on the quality of a pedigree. We implemented a PCI computation algorithm as used in the PEDIG package by Boichard (2002). Instead of 8th generation tracking through PEDIG package, *PedGetF* module can produce upto PCI upto 5th generation. Note that an additional argument is required for obtaining PCI estimates in the output file.



ANGELPED (Pedigree Get_F Module)

PED-GetF

Pedigree file: path/to/input/file

I/O File options

Input File Type
● Free format
○ Fixed format

	Animal	Sire	Dam
Starts at			
Length			

Input file delimiter
● Space(s)
○ Tab(s)
○ Comma(s)
○ Others

Missing Value: 0

Output file delimiter
● Space(s)
○ Tab(s)
○ Comma(s)
○ Others

Others
□ Show hash information
□ Treat ID as numeric
☑ Repeated delim. as one
□ Use Tabular method algorithm
□ Print renumbered pedigree
□ Print pedigree completeness index

Output file: path/to/output/file

Figure 5. The front-end GUI for *PedGetF* module.

Availability, platform compatibility and installation

AngelPedTK 1.0 software toolkit can be freely downloaded from http://www.nias.go.kr/. Both command line modules and modules with GUI wrappers are Windows platform specific and are distributed in both 32- and 64 bits formats. These are compiled binaries, complied by GNU gcc and Qt/C++ compilers. The GUI distribution provides all required Windows DLL files, so that it can be run without prior installation on user computers. We, however, do not provide Linux binaries but source codes are available by request for platform specific compilation.

Special GUI Features

The GUI of AngelPedTK 1.0 software implemented some convenient Windows OS specific features such as file browsing, "drag and drop" for file inputs, native windows look with Qt framework. The GUI includes a dedicated dashboard to provide a preview on the input and log files. This kit can utilize the system default text file editors (i.e. notepad) for previewing large output files and system default internet browsers to invoke help pages. Another helpful feature of the GUI module is the auto generation of output file names with respect to input files which, of course, can be modified easily according to user demands.

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