Disaster Victim Identification app: dviapp

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This app deals with Disaster Victim Identification (DVI) problems and power calculation for kinship problems. Our goal has been to make available functionality in the `pedsuite` of R libraries and also the `dvir` library. Compared to `Familias`, the app provides several extensions including more general conditional simulations, exclusion calculations and the ability to handle multiple missing persons in a family.

Here's the dviapp: https://thoree.shinyapps.io/dviapp/

There are several built-in-cases. Alternatively, users can run run their own examples by uploading Familias files or data on R format.

There are tree modules:

- Power: Simulations can be done to determine if the statistical evidence is sufficient.
- Priority: The aim is to find the optimal extra persons to genotype in cases with insufficient data.
- DVI: Methods to include or exclude missing persons are provided.

These modules are explained and exemplified below. For more information, please check the books Mass identications (Kling et al., 2021), Pedigree Analysis in R (Vigeland, 2021), or the dvir paper (Vigeland and Egeland, 2021). For further documentation and bug reporting, please go here.

Mutations are switched off in the examples below if not stated otherwise. However, mutation can be turned on in `Settings` and other options can be changed there as well.

Power

Power calculations are generally performed prior to the actual analysis to determine if there is sufficient data to reach conclusions. The conclusion from a power analysis may be that there is sufficient information *or* that we are not likely to reach reliable conclusions. In the latter case more data is needed, either more markers or more genotyped reference individuals. This is explored in the `Prioritise` module.

We consider two hypotheses

- H_1: The Person Of Interest (POI) is the Missing Person (MP).
- H_2: POI is unrelated to MP.

The hypotheses are illustrated below.

Marker data is simulated a specified number times for POI and the references (in the figure above there is only one reference). The default number of simulations is 100 and should be increases to 1000 in final applications. The simulations are done conditionally on genotyped individuals, above there are none. These simulations are done assuming H_1 to be true, i.e., assuming that POI is MP. For each of these simulations the LR is calculated. This gives values $LR_1, \dots, LR_{100}$ and based on these values, the app produces the plot:

The left panel shows that the mean $\log_{10}$(LR) is 6.24, which corresponds to mean LR equal to 1,737,801. From the panel on the right hand side, we see that $\log_{10}$(LR) exceeds 3.89 with probability 0.8, or equivalently LR exceeds 7762 with probability 0.8. If the requirement is that LR should exceed 10,000 with a probability of at least 0.8, the power is not quite satisfactory.

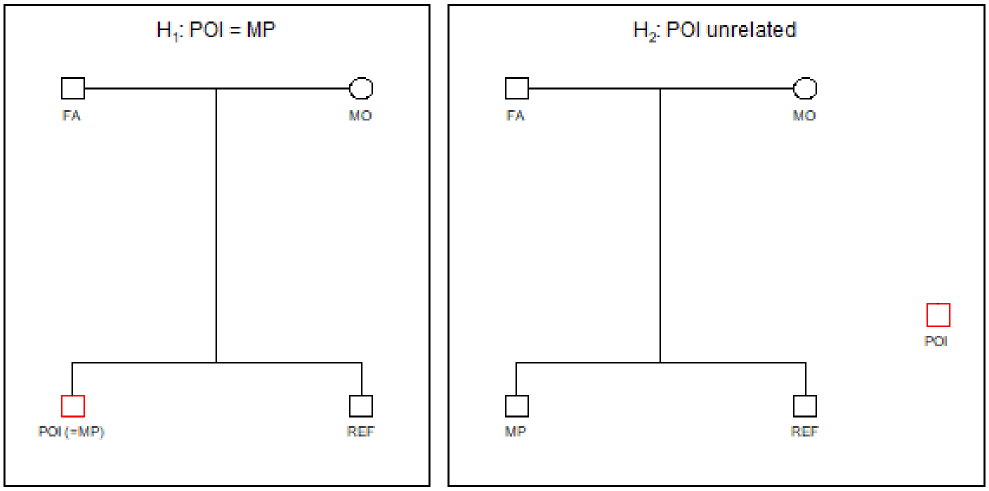


Figure 1: Hypotheses in missing person case

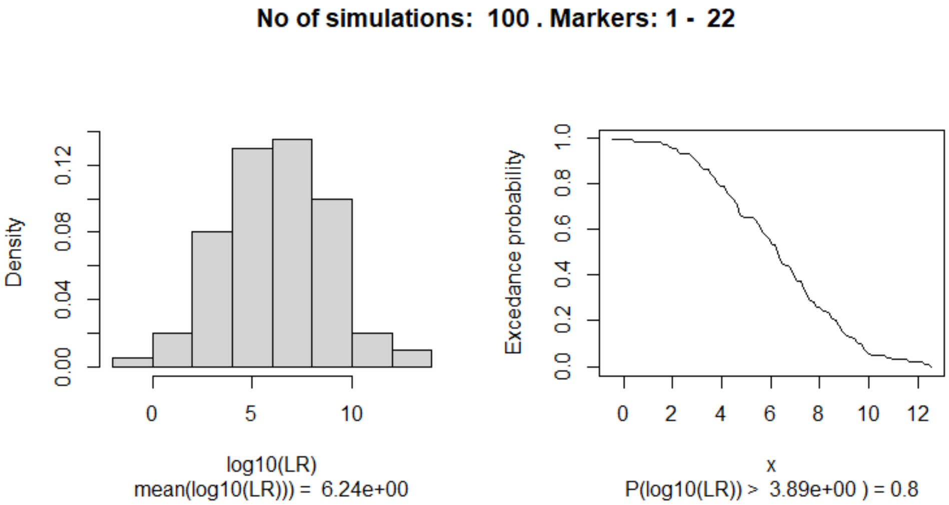


Figure 2: Distribution of log10(LR)

Analyses based on built-in-cases

For the built-in part, 35 markers from the `NorwegianFrequency` database (documented in the R library `forrel`) are used. Above, the 22 first markers have been selected. If the number of markers is increased to 25 in the above example, the threshold of 10,000 is met.

Greater accuracy, at the cost of increased computational time, is obtained by increasing the number of simulations in `Settings`. To obtain the same sequence of simulations, and the same result for repeated calculations, the `Seed` in `Settings` need to be set to same value.

Analyses based on user loaded data

The analyses in this window is the same as explained above. The difference is that the data is now loaded from a Familias file. The file is created on before hand in the main module of Familias, not the DVI module of Familias. The missing person need to be named `MP` and the reference `REF`. These individuals are not genotyped. There may be genotyped individuals. If so, these will be conditioned on in the simulation. The genotyped individuals will be hatched in the plot and the first marker is displayed.

Prioritise

The typical scenario for this functionality is as follows: A power calculation has been performed. The conclusion is that more individuals need to be genotyped in the hope of reaching sufficient power. We consider alternatives where extra family members `E1` and `E2` are available. Results are reported when `E1` is genotyped and both `E1` and `E2`. In addition to the LR distribution described previously, results are also given for the `Exclusion probability` (EP) explained below.

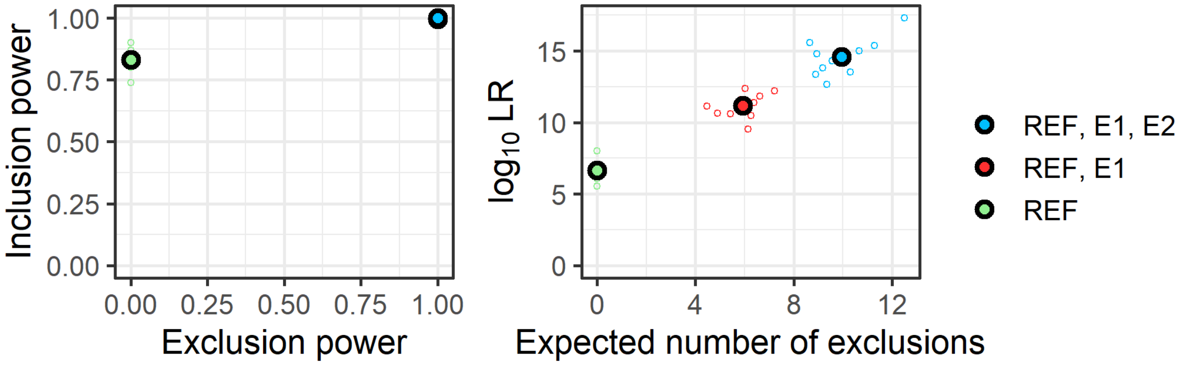


Figure 3: Prioritise plot

Consider first the panel on the left hand side. The Y-axis gives the inclusion power (IP) defined as the probability that LR exceeds 10,000 given H_1, i.e., `MP = POI` is true. If only the member `REF` of the the reference family is genotyped, IP is close to 0.8. In this case, ten profiles for `REF`, `E1` and `E2` have been simulated. For each of these profiles, 100 simulations are performed for `MP` under H_1 and H_2. The smaller circles in the plot correspond to these 10 profile simulations while the larger circles represent averages. For both other alternatives, (`REF`, `E1`), and (`REF`,`E1, E2`), IP is very close to 1.

The Y-axis in the panel to the right, shows the alternative (`REF`,`E1, E2`) to be the most powerful, as expected. The X-axes give information on `EP`. The baseline alternative, with only `REF` genotyped, gives the values 0 in both plots. This is obvious, since exclusion is not possible if only one brother is genotyped as two brothers need not share alleles. If there are more than two brothers, exclusion is indicated if more than four alleles are observed. Mutations are disregarded for exclusion calculations. If additional brothers are genotyped, exclusion is probable and also likely as evidenced by EP in the plot to the left and by the expected number of exclusions to the right.

As for the Power module, simulations can be done either for built-in-cases or by loading a Familias file.

DVI

Also in this module, analyses can be done from built-in-cases or from Familias files. In addition R-data can be loaded provided they are on the same format as the examples in the dvir library. The below figure shows the planecrash data.

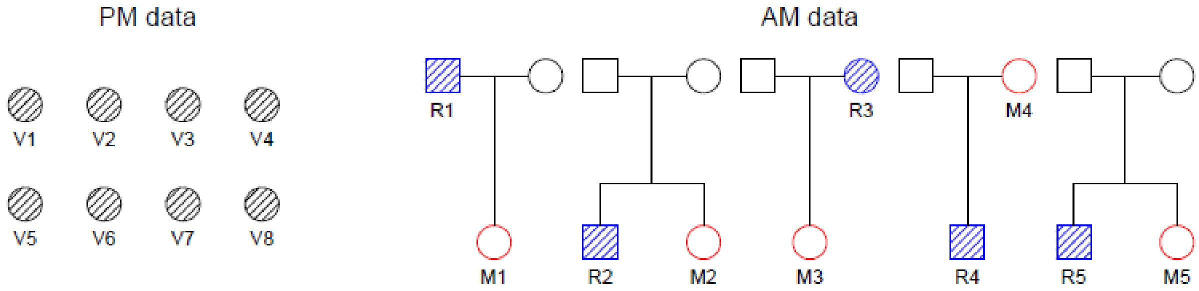


Figure 4: Planecrash example

There are 8 female victims to left, hatched since they are genotyped. To the right there are five reference families, each having one missing person and one reference family member. In the following sections, we explain possible analyses based on the planecrash data to exemplify.

For analyses involving AM data based on Familias files, relabeling of the names of the missing persons is required, i.e., the user needs to tick Relabel. The reason is that all missing persons by default have the same name in the fam file.

IBD estimates

This part deals with identical by descent (IBD) coefficients quantifying relatedness. The distinction between alleles identical by descent (IBD) and alleles identical by state (IBS) is essential. IBD alleles originate from the same ancestral allele within a given pedigree, while IBS alleles only have the same appearance, but they need not come from the same ancestor. Unrelated individuals may share IBS alleles, but not IBD alleles.

The relationship between a pair of non-inbred individuals can be described in more detail by Z, the number of IBD alleles shared by two individuals. We define the IBD coefficients

$$\kappa_0 = P(Z = 0),\ \kappa_1 = P(Z = 1),\ \text{and}\ \kappa_2 = P(Z = 2).$$

The corresponding estimates are denoted k0, k_1 and k2.

The pairwise relationship between all pairs of victims is estimated and compared to unrelated. Here's an example:

```
##    id1 id2  N        k0         k1        k2           LR
## 28  V7  V8 15 0.1401716 0.56471243 0.2951160 7.375616e+05
## 12  V2  V7 15 0.5171441 0.36534023 0.1175156 4.425561e+01
## 19  V4  V5 15 0.7892599 0.01978912 0.1909510 1.307272e+01
## 7   V1  V8 15 0.5214316 0.47856843 0.0000000 1.246938e+01
## 14  V3  V4 15 0.6412325 0.35876747 0.0000000 8.847521e+00
```

There are $7 \cdot 8/2 = 28$ pairwise comparisons that can be made between the 8 victims. Above, five are listed, sorted according to decreasing LR.

The parameters describing the pairwise relationship are estimated as (k0 = 0.14, k1 = 0.56, k2= 0.30). This is quite far from the parameters describing unrelated individuals, (0, 1, 0). The LR tests the estimated relationship against the specified, unrelated in this case. In this case, $LR = 737562$, and this provides strong evidence in favor of V7 and V8 being related.

Exclusion

Each victim is tried in each missing person position and the number of exclusions are counted. The results are summarised in the `exclusion matrix` below:

```
##    M1 M2 M3 M4 M5
## V1  0  0  8  9  0
## V2  4  0  0  7  0
## V3  7  0  8  1  0
## V4  3  0  6  6  0
## V5  2  0  6 10  0
## V6  5  0  3  5  0
## V7  7  0  2  7  0
## V8  6  0  6  6  0
```

We see that families 2 and 5, with missing persons M2 and M5, do not allow for exclusions as only one sibling has been genotyped. The corresponding columns therefore only contain 0-s. Furthermore, we see that the only likely candidate for M1 is V1, since for the other victims there are at least two exclusions.

Pairwise LR

For each victim V and each missing person M, the LR comparing `V = M` to `V and M unrelated`, is calculated. Here's an example :

```
##              M1           M2           M3           M4           M5
## V1 9.248816e+02 9.411564e-04 1.258106e-22 2.750399e-26 2.853849e-01
## V2 1.500072e-10 6.928184e-02 6.739736e+04 2.332834e-19 6.864631e-02
## V3 2.698238e-20 1.073578e-04 6.307786e-23 2.493147e+02 3.983652e-03
## V4 9.962125e-07 3.957145e-05 2.162647e-15 1.141707e-15 3.169369e+07
## V5 9.090162e-02 9.994029e-04 3.844531e-17 3.649795e-29 4.065066e-03
## V6 9.507818e-14 1.069007e+06 1.012061e-07 1.273562e-14 1.356608e-05
## V7 9.168642e-19 6.155248e-04 4.982251e+00 4.512892e-20 1.959095e-01
## V8 4.634759e-16 1.998729e-04 3.193541e-14 1.773908e-16 2.801497e-01
```

A mutation model has been defined (the proportional model with rate = 0.001) and so all likelihood ratios are positive. We see that the only candidate for the missing person M1 is V1, the LR is 925, all other LR-s are close to 0. If mutations are removed, we get

```
##          M1           M2       M3 M4           M5
## V1 928.6003 9.033557e-04     0.00  0 2.772464e-01
## V2   0.0000 6.745912e-02 67917.21  0 6.663941e-02
## V3   0.0000 1.030688e-04     0.00  0 3.820204e-03
## V4   0.0000 3.779779e-05     0.00  0 3.189844e+07
## V5   0.0000 9.623366e-04     0.00  0 3.921652e-03
## V6   0.0000 1.079809e+06     0.00  0 1.293453e-05
## V7   0.0000 5.901476e-04     0.00  0 1.904472e-01
## V8   0.0000 1.910791e-04     0.00  0 2.722293e-01
```

Joint

All possible assignments of victims to missing persons, are evaluated and solutions are ranked according to the likelihood ratio. Here's an example

```
##   V1 V2 V3 V4 V5 V6 V7 V8    loglik           LR   posterior
## 1 M1 M3  * M5  * M2  *  * -562.8019 2.172326e+21 0.998924269
## 2  * M3  * M5  * M2  *  * -569.6356 2.339356e+18 0.001075731
```

The best solution is the assignment where V1 = M1, V2 = M3, V4 = M5 and V6 = V2. The remaining victims, V3, V5, V7 and V8 are not identified. This optimal solution has an LR of $2.2 \cdot 10^{21}$ compared to the assignment where no victims are identified. The rightmost column gives the posterior probability. It can be shown that there are 19081 apriori possible assignments, i.e., there are 19081 possible ways of identifying victims and missing persons when data is not taken into account. Each of these assignments are given a prior probability of 1/19081. The posterior is then calculated using Bayes Theorem.

If mutations are modelled, the five best candidate assignments are

```
##   V1 V2 V3 V4 V5 V6 V7 V8    loglik           LR    posterior
## 1 M1 M3 M4 M5  * M2  *  * -557.3114 5.265386e+23 9.947433e-01
## 2 M1 M3  * M5  * M2  *  * -562.8301 2.111943e+21 3.989910e-03
## 3  * M3 M4 M5  * M2  *  * -564.1411 5.693038e+20 1.075536e-03
## 4  * M3 M4 M5 M1 M2  *  * -566.5391 5.175064e+19 9.776795e-05
## 5 M1  * M4 M5  * M2 M3  * -566.8239 3.892360e+19 7.353495e-05
```

This gives the additional identification, V3 = M4. Note that the exclusion matrix presented earlier displayed only one inconsistency for V3 being M4.

Posterior

This functionality is most easily explained by an example:

```
##              M1 M2           M3           M4 M5            *
## V1 9.988219e-01  0 2.198990e-30 1.294484e-31  0 1.178114e-03
## V2 1.437796e-17  0 9.999112e-01 8.271431e-26  0 8.875304e-05
## V3 1.164115e-25  0 3.738601e-30 9.960050e-01  0 3.994971e-03
## V4 0.000000e+00  0 0.000000e+00 0.000000e+00  1 0.000000e+00
## V5 9.816881e-05  0 5.703210e-22 1.457939e-31  0 9.999018e-01
## V6 0.000000e+00  1 0.000000e+00 0.000000e+00  0 0.000000e+00
## V7 9.900903e-22  0 7.391698e-05 1.802754e-22  0 9.999261e-01
## V8 5.005288e-19  0 4.737957e-19 7.086710e-19  0 1.000000e+00
```

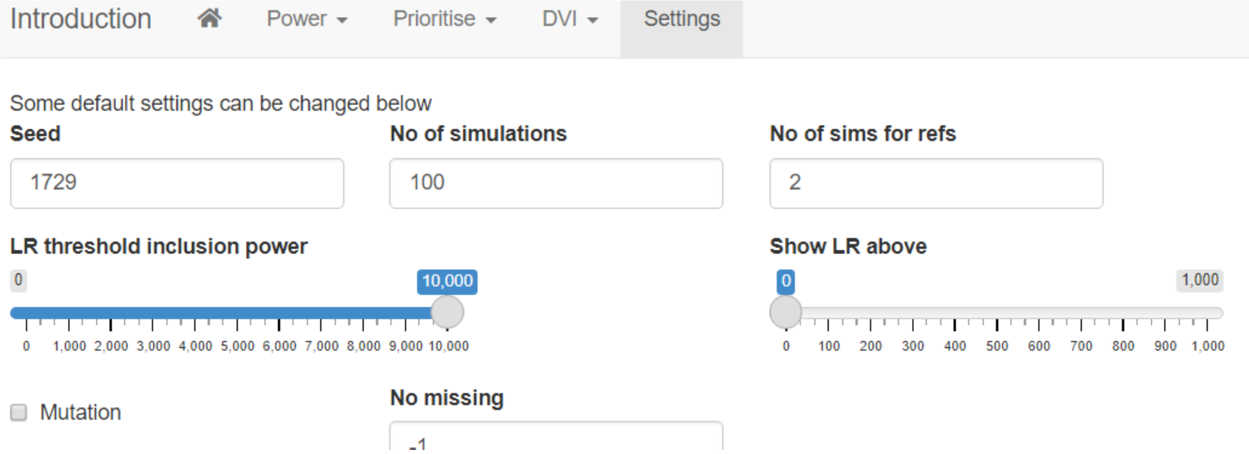
The output shows that $P(V1 = M1) = 0.9988$ while V1 is someone unrelated with probability 0.0012. Note that the probabilities of each line sum to 1.

Settings

The settings are shown in the below figure:

The options are:

- `Seed:` Use the same seed to secure the same simulation results.
- `No of Simulations:` The default of a 100 may be increased to obtain more accurate results.
- `No of sims for references:` This only applies to the `Prioritise module`. The indicated number (default is 2) of profiles are simulated for the relatives, assuming H1. For each of these profiles, the specified number of simulations are performed for `MP` under H1 and H2.
- `LR threshold inclusion power:` This only applies to the `Prioritise module`. If the threshold is x, the default is 10,000, the inclusion power is $P($ LR$ > x | H_1)$.
- `Show LR above:` Some tables in the DVI module may be large. They may reduced by only displaying output where the LR exceeds the specified value.
- `Mutation:` By default mutation is not accounted for. It may be turned on. Obviously, if there is no mutation in user input, this will have no impact.
- `No of missing:` If any reference family contains more than one missing, the total number of missing must be given here. Also, in this case the missing persons should be named M1, M2, … in the Familias file.



Some default settings can be changed below

Seed: 1729

No of simulations: 100

No of sims for refs: 2

LR threshold inclusion power: 0 – 10,000

Show LR above: 0 – 1,000

□ Mutation

No missing: -1

Figure 5: Settings