

CaseSolver

A program based on EuroForMix for
analysing case data.

Version 1.0.0 (compiled June 2018)

by Øyvind Bleka, Oslo University Hospital

About

- A R-program with many functionalities
- Most important is profile comparisons:
 - References to evidence profiles.
 - Single source profiles to other evidence profiles.
 - Can utilize peak heights.
- Mixture comparison follows strategy given in



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dnamatch2: An open source software to carry out large scale database searches of mixtures using qualitative and quantitative models

Ø. Bleka ^a, M. Bouzga ^a, A. Fonneløp ^a, P. Gill ^{a, b}

- Suitable for cases with large amount of profiles.
- Detailed mixture analyzes using EuroForMix.
 - Advanced deconvolution module
 - Show "Model fitted Peak heights"
- Customize friendly:
 - Design your own data import function!
 - Many kits supported.
 - Design your own strategy/report.

Installation

Requirements/Startup



- Software R installed (newer than version 3.0.1)

<https://cran.r-project.org/>

- R-packages installed:

- The R-package casesolver
- The R-package euroformix ($\geq 1.10.0$)
- Other R-packages:

```
install.packages(c("gWidgets2tcltk","R2HTML","igraph"))
```

- Done only first time.

- Startup:

- Open R and type (copy-paste command)
`library(casesolver);gui()`

Installing casesolver

Copy and run (press ENTER) these commands in the R-software (example with casesolver version 1.0.0):

```
install.packages("devtools")  
library(devtools)  
install_github("oyvble/casesolver/casesolver_1.0.0")
```

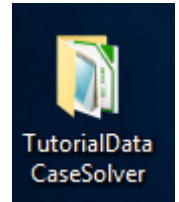
You can also install euroformix in same manner (version 1.11.4):
`install_github("oyvble/euroformix/euroformix_1.11.4")`

Demonstration using CaseSolver with example

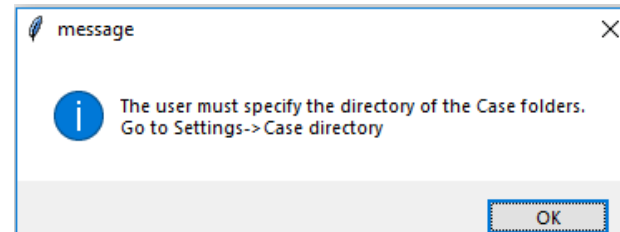
A ESX17 toy example

Setting up CaseSolver for analyzing tutorial data

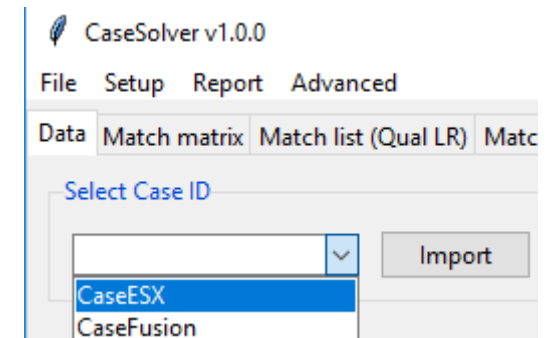
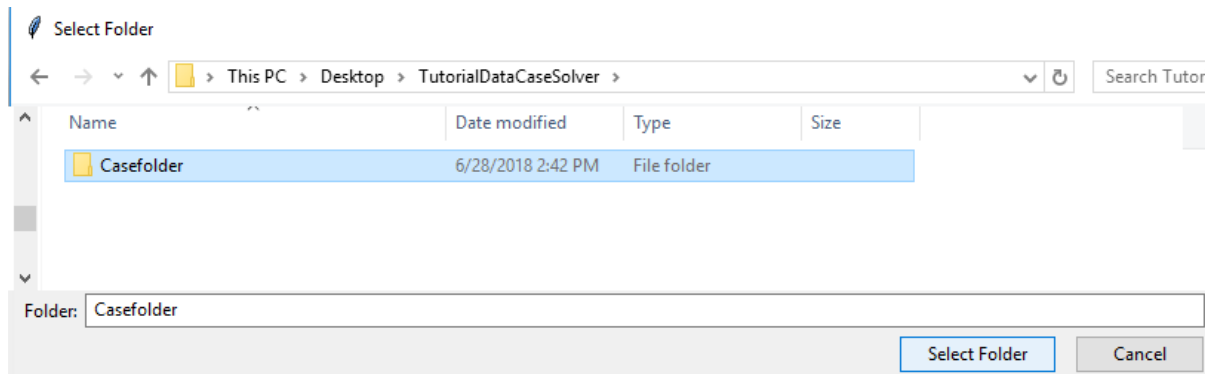
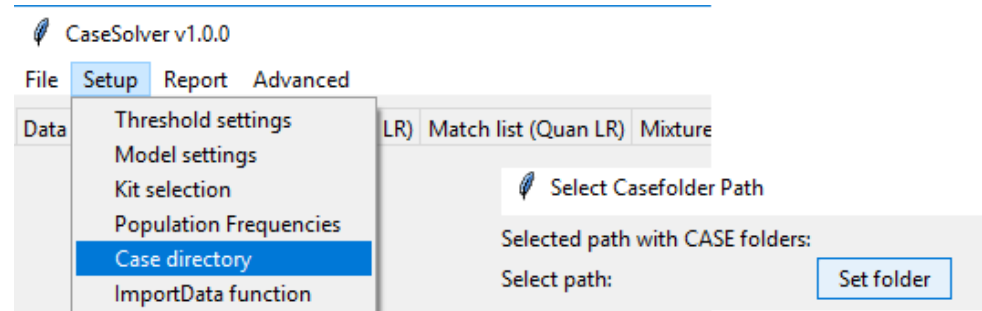
1) Extract folder *TutorialDataCaseSolver* from zip-file to the desktop.



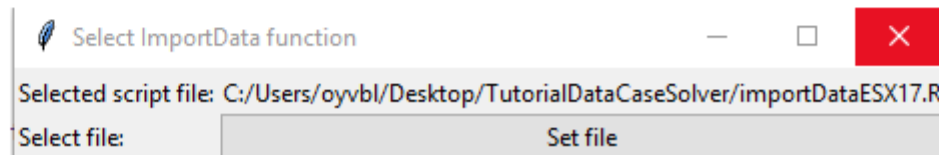
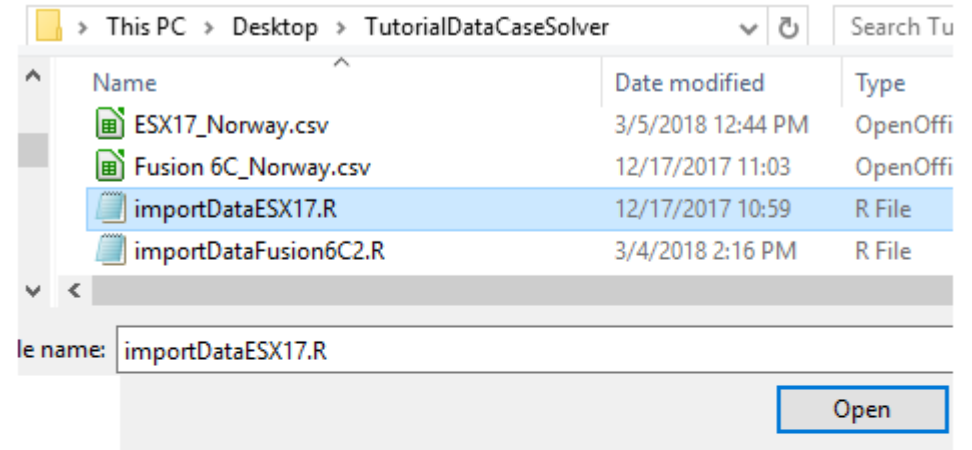
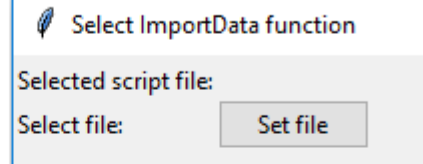
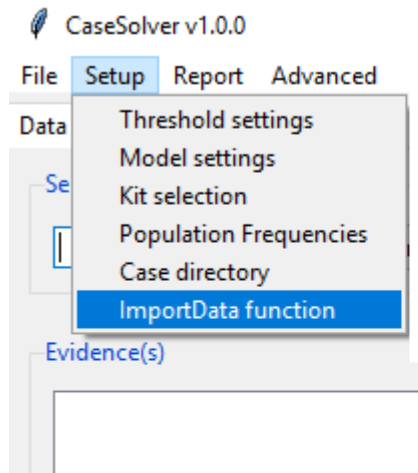
2) Open R and copy-paste this command:
`library(casesolver);gui()`



3) Select CaseDirectory



4) Select ImportData function



4) Select frequency file

The image shows the 'CaseSolver v1.0.0' application interface. The 'Setup' menu is open, and 'Population Frequencies' is selected. A file selection dialog is also open, showing the file 'ESX17_Norway.csv' selected in the 'TutorialDataCaseSolver' directory. The dialog includes a table of files and an 'Open' button.

CaseSolver v1.0.0

File Setup Report Advanced

Data

Se

Threshold settings
Model settings
Kit selection
Population Frequencies
Case directory
ImportData function

Evidence(s)

Select population frequency file

Selected frequency file:

☒ Include AMEL

Select file

View frequencies

Select file

← → ^ ↑ > This PC > Desktop > TutorialDataCaseSolver > ↻

Name	Date modified	Type
Casefolder	6/28/2018 2:42 PM	File folder
ESX17_Norway.csv	3/5/2018 12:44 PM	OpenOffi
Fusion 6C_Norway.csv	12/17/2017 11:03	OpenOffi
importDataFSX17.R	12/17/2017 10:59	R File

File name: ESX17_Norway.csv

Open

Select population frequency file

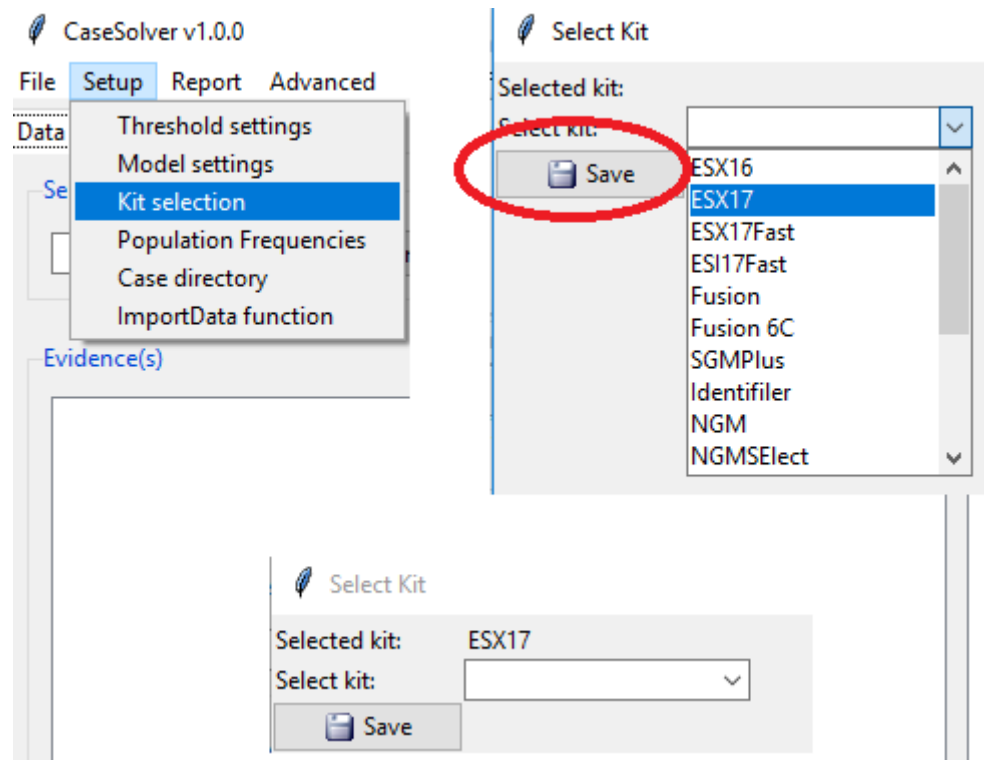
Selected frequency file: C:/Users/oyvbl/Desktop/TutorialDataCaseSolver/ESX17_Norway.csv

☒ Include AMEL

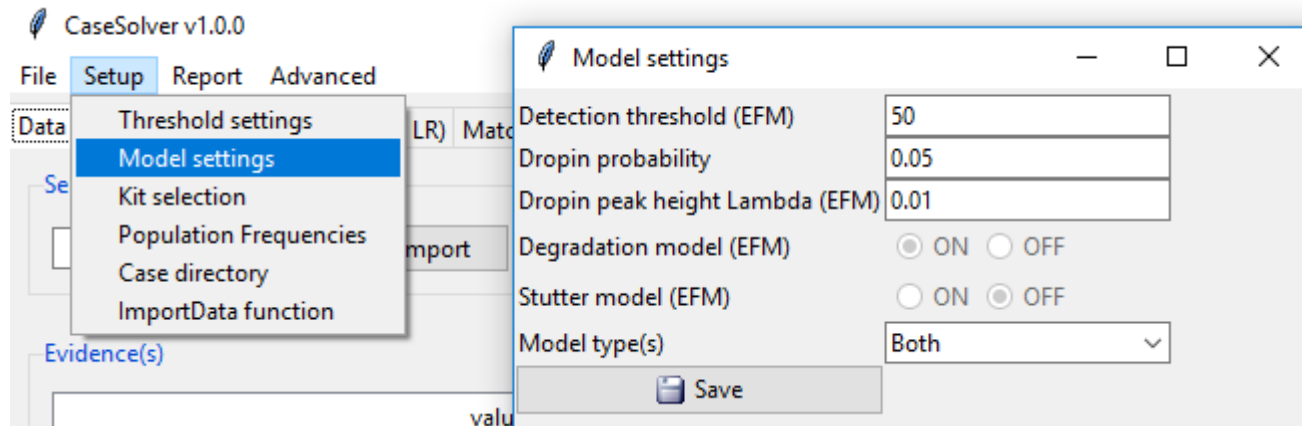
Select file

View frequencies

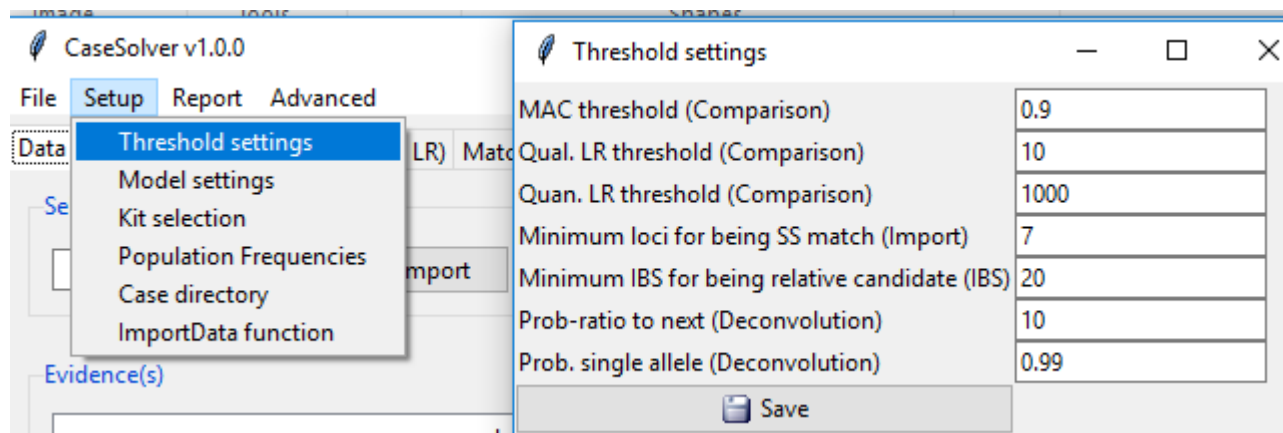
5) Select Kit (can be changed any time):



6) Select Model settings (use default)



7) Select Threshold settings (use default)



The user interface after importing data from a case

Click "import"

CaseSolver v1.0.0

File Setup Report Advanced

Data Match matrix Match list (Qual LR) Match list (Quan LR) Mixtures Deconvoluted

Select Case ID

CaseESX Import ☒ Sort Evids by # ☐ Sort Evids by Sample.ID ☒ Sort Refs by # ☐ Sort Refs by Sample.ID

Evidence(s)

ID	SampleName	MatchStatus	AMEL	D3S1358	TH01	D21S11	D
#1	S3	Unknown 1	X/Y	16/18	6/7	30/31.2	14
#2	S5	ref3	X/Y	16/18	6/8	28	14/
#3	S1	ref2	X	15/18	6/9.3	28/31	12/
#4	S2	ref1	X	16/17	6/8	30.2/31.2	12/
#5	S4	mixture	X	15/16/17/18	6/8/9.3	28/30.2/31/31.2	12/
#6	S6	mixture	X/Y	14/15/16/18	6/8/9.3	28/30/31.2	14/

Reference(s)

ID	SampleName	AMEL	D3S1358	TH01	D21S11	D18S51	D10S12	D1S1656	D
#1	ref1	X/X	16/17	6/8	30.2/31.2	12/14	13/16	16.3/17.3	
#2	ref2	X/X	15/18	6/9.3	28/31	12/15	13/15	17/17.3	
#3	ref3	X/Y	16/18	6/8	28/28	14/16	15/16	10/17.3	
#4	Unknown 1	X/Y	16/18	6/7	30/31.2	14/14	13/16	12/15	

Functionalities

Compare Create Report Add reference profile Export profile(s) Calculate RMP Calculate IBS Restart

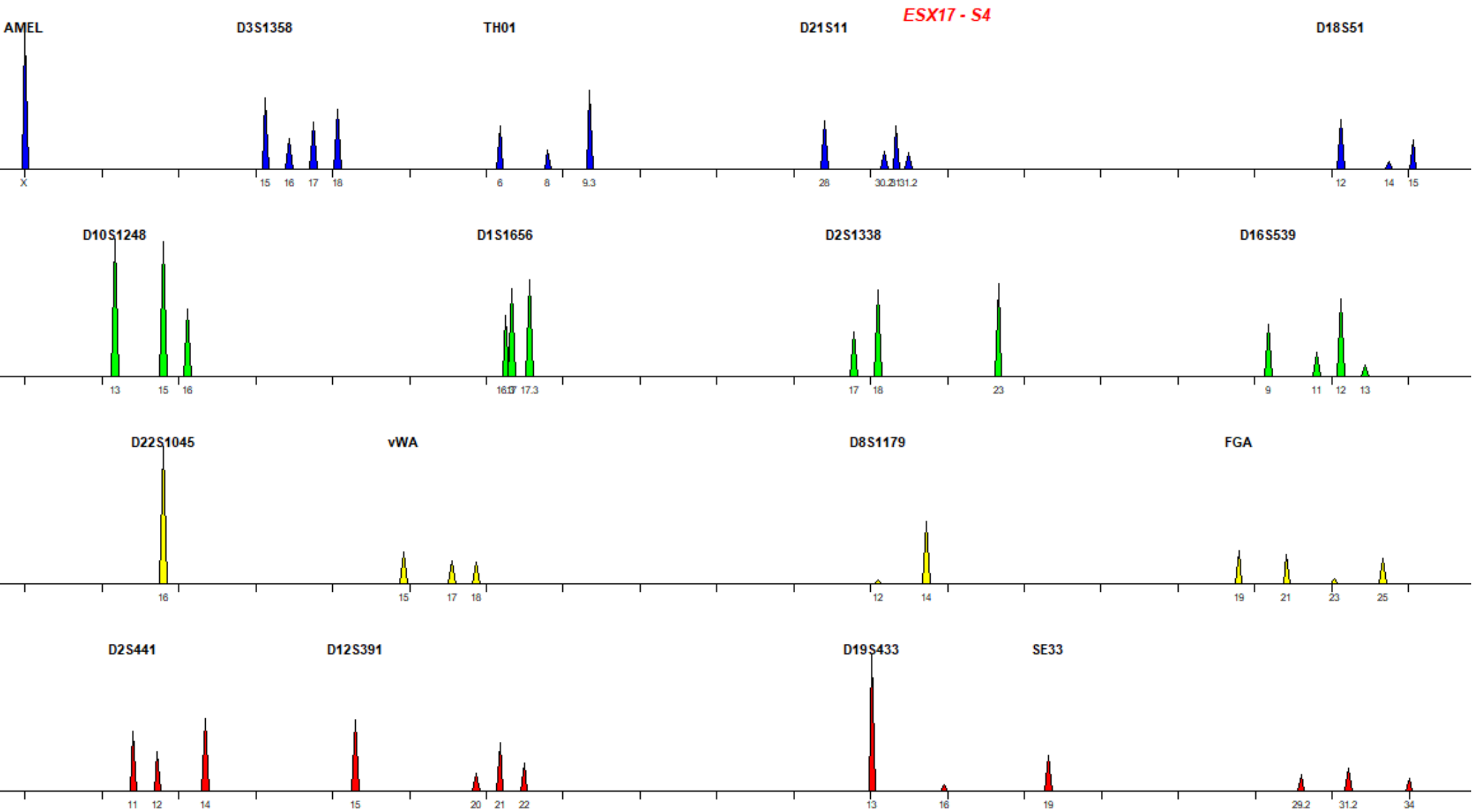
Automatical identification by case-import

Evidence(s)								Reference(s)								
ID	SampleName	MatchStatus	AMEL	D3S1358	TH01	D21S11	D	ID	SampleName	AMEL	D3S1358	TH01	D21S11	D18S51	D10S12	D1S1656
#1	S3	Unknown 1	X/Y	16/18	6/7	30/31.2	14	#1	ref1	X/X	16/17	6/8	30.2/31.2	12/14	13/16	16.3/17.3
#2	S5	ref3	X/Y	16/18	6/8	28	14/	#2	ref2	X/X	15/18	6/9.3	28/31	12/15	13/15	17/17.3
#3	S1	ref2	X	15/18	6/9.3	28/31	12/	#3	ref3	X/Y	16/18	6/8	28/28	14/16	15/16	10/17.3
#4	S2	ref1	X	16/17	6/8	30.2/31.2	12/	#4	Unknown 1	X/Y	16/18	6/7	30/31.2	14/14	13/16	12/15
#5	S4	mixture	X	15/16/17/18	6/8/9.3	28/30.2/31/31.2	12/									
#6	S6	mixture	X/Y	14/15/16/18	6/8/9.3	28/30/31.2	14/									

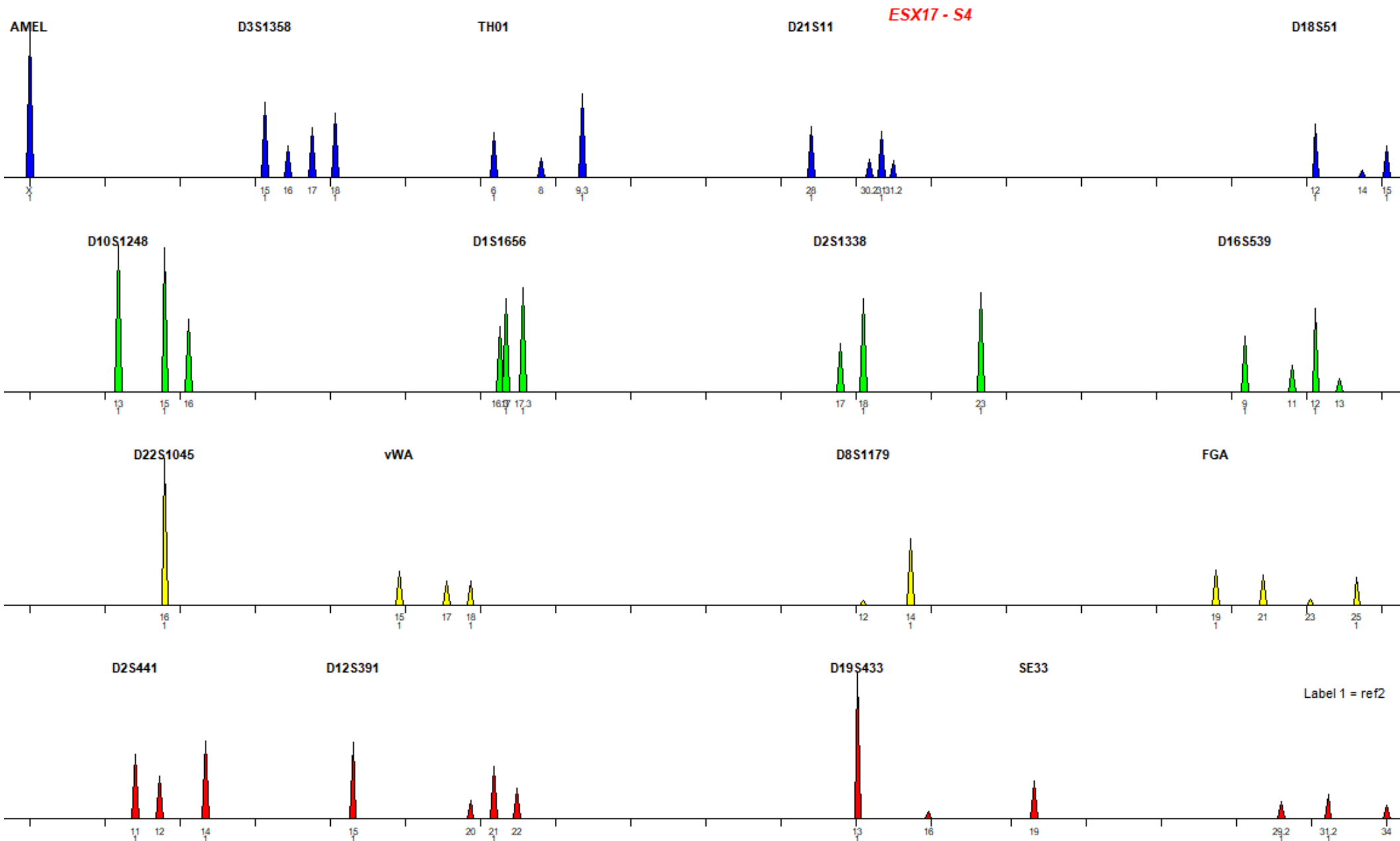
Every reference is compared to evidence profiles classified as “non-mixture”.

- Matching refs identified and labeled in MatchStatus.
 - Supports missing loci
- Otherwise assigned as an unknown
 - Added to Reference list
 - Consensus creation of unknowns

Double-clicking profiles gives EPG

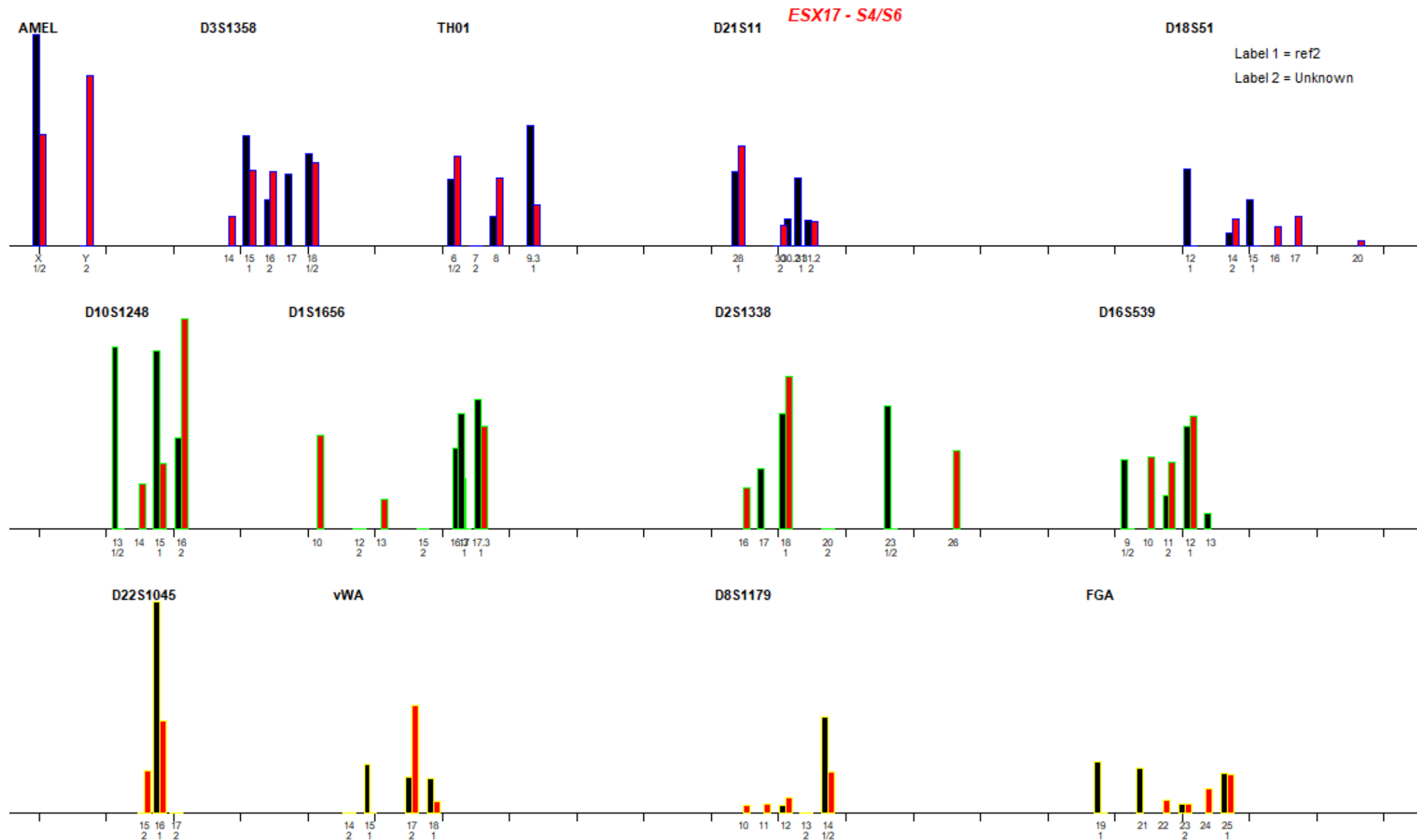


Double-clicking ref-profiles to show

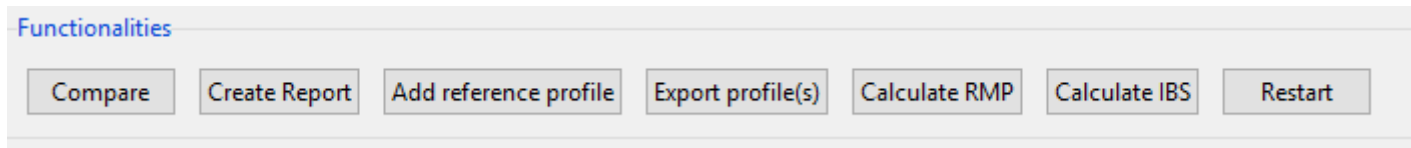


Multiple profiles

Hold CTRL to select multiple profile. Then press ENTER.



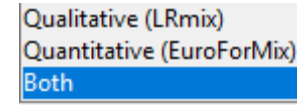
Functionalities



- **Compare:** Comparing all refs to mixtures.
 - Allele comparison + LR (LRmix) + LR (EuroForMix)
- **Create Report:** Creates a HTML based report (data+comparisons).
- **Add reference profile:** Add/remove reference profiles
- **Export profile(s):** Export evidence/reference profiles to a text-file or directly to EuroForMix.
- **Calculate RMP:**
 - Random match probability calculated for all references.
 - RMNE calculated for all evidences.
- **Calculate IBS:** Gives number of shared alleles between pairwise compared reference profiles

Comparison

Compare



Compare performs 2 steps to retrieve candidate matches:

Step 1: Simple allele comparison

Step 2: LR based comparison

Step 2 can be done in 3 different variants:

- (a) LR based only on qualitative model (LRmix)
 - (b) LR based only on quantitative model (EuroForMix)
 - (c) Both: First (a) and then (b).
-
- (a) is very fast and (b) can be very slow.
 - (a) is useful as a prefilter for (b).

Set threshold for candidate match

Compare relies on specified thresholds

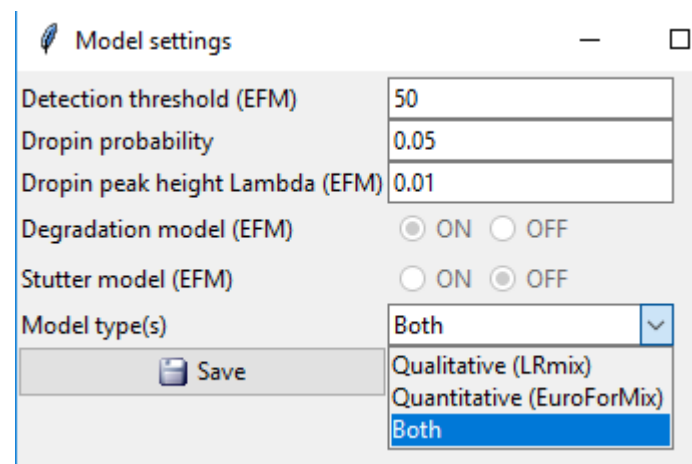


Threshold settings

MAC threshold (Comparison)	0.9
Qual. LR threshold (Comparison)	10
Quan. LR threshold (Comparison)	1000

Model choice of Step 2 can be selected here:

Variant (c) is default (Both)



Model settings

Detection threshold (EFM)	50
Dropin probability	0.05
Dropin peak height Lambda (EFM)	0.01
Degradation model (EFM)	<input checked="" type="radio"/> ON <input type="radio"/> OFF
Stutter model (EFM)	<input type="radio"/> ON <input checked="" type="radio"/> OFF
Model type(s)	Both

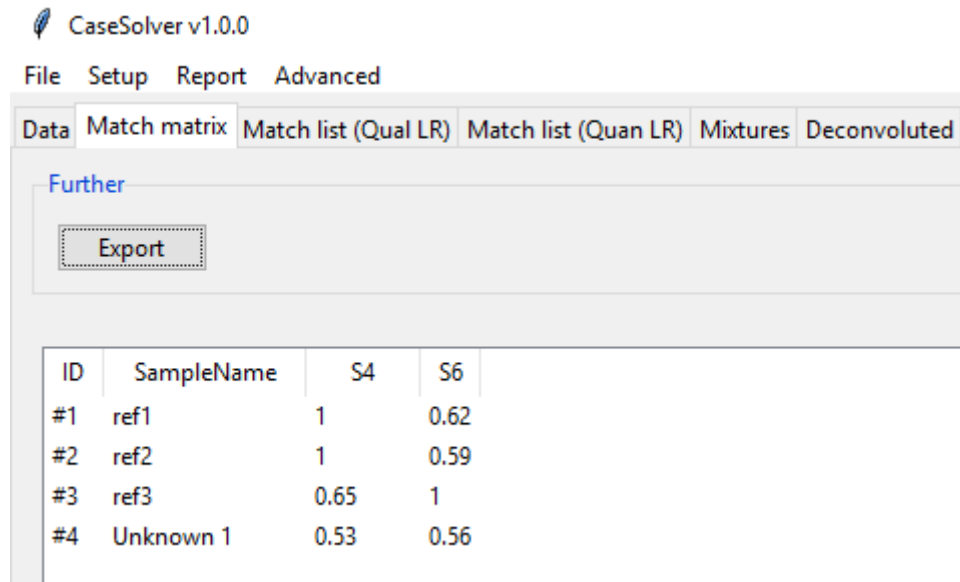
Save

- Qualitative (LRmix)
- Quantitative (EuroForMix)
- Both

Step 1

All reference profiles are allele-compared against all mixtures.

- Score = Proportion of alleles of ref which is included in a mixture (MAC)
- Score for all combination given in Match matrix (can be exported):



CaseSolver v1.0.0

File Setup Report Advanced

Data Match matrix Match list (Qual LR) Match list (Quan LR) Mixtures Deconvoluted

Further

Export

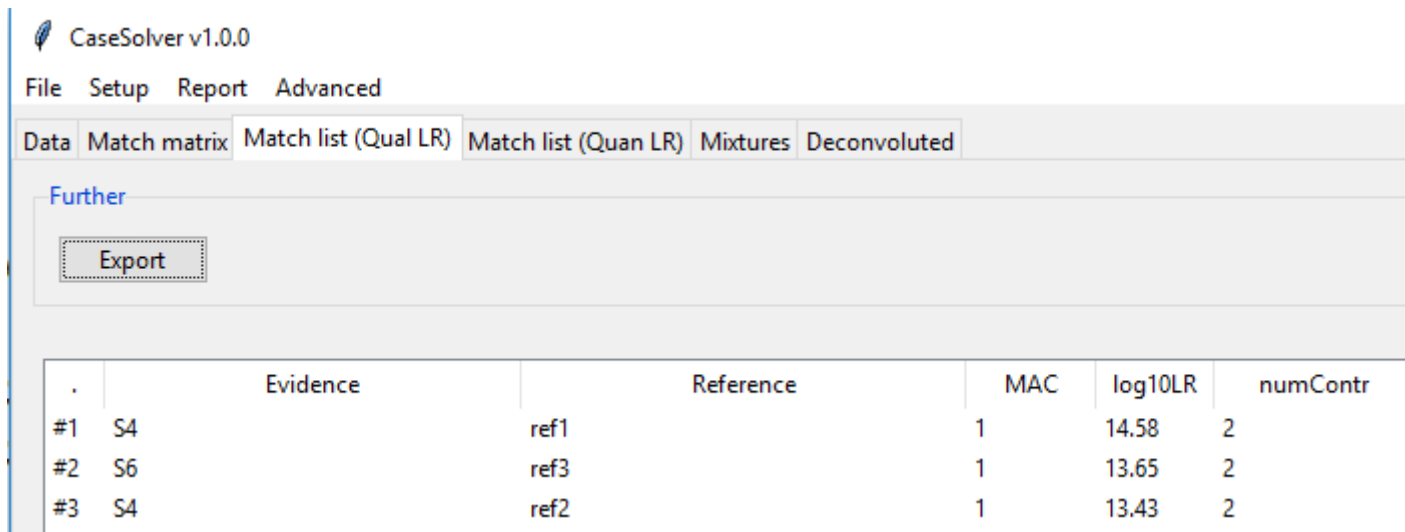
ID	SampleName	S4	S6
#1	ref1	1	0.62
#2	ref2	1	0.59
#3	ref3	0.65	1
#4	Unknown 1	0.53	0.56

All candidate matches (with Score>threshold) provided to step 2.

Step 2a

Calculating ML based LR for the candidate matches (Qual model)

- Addition: Estimates number of contributors in evidence.
- LR for all comparisons given in Match list (Qual LR) can be exported



The screenshot shows the CaseSolver v1.0.0 application window. The 'Match list (Qual LR)' tab is selected. Below the tabs, there is a 'Further' section with an 'Export' button. A table displays the match list data.

	Evidence	Reference	MAC	log10LR	numContr
#1	S4	ref1	1	14.58	2
#2	S6	ref3	1	13.65	2
#3	S4	ref2	1	13.43	2

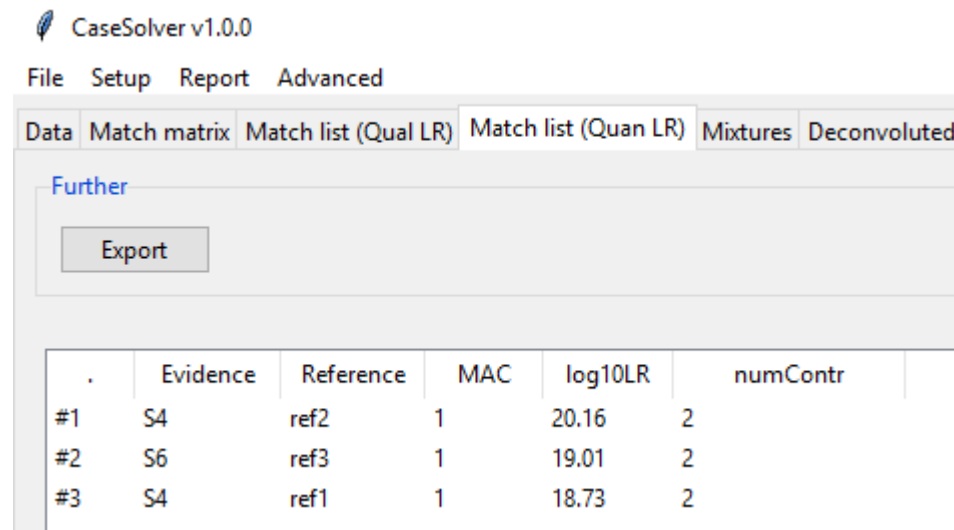
All candidates with $LR > \text{threshold}(\text{qual})$ are candidate matches.

Provided to Step 2b if selected.

Step 2b/c

Calculating ML based LR for the candidate matches (Quan model)

- LR for all comparisons given in Match list (Quan LR) can be exported

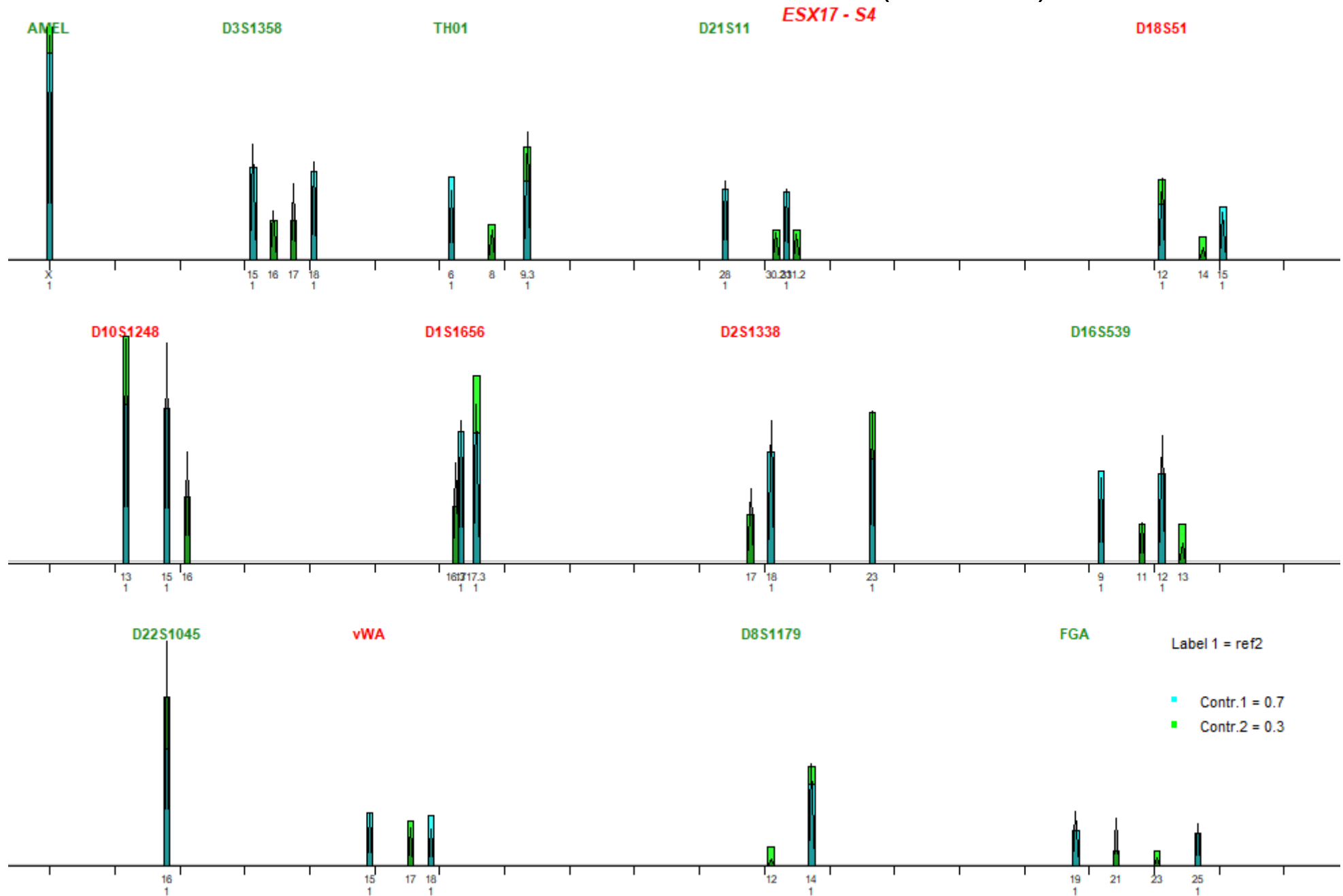


All candidates with $LR > \text{threshold}(\text{quan})$ are candidate matches.

Note: Candidates can be double-clicked on to see
"Model fitted Peak heights"

Evaluating candidates in match list

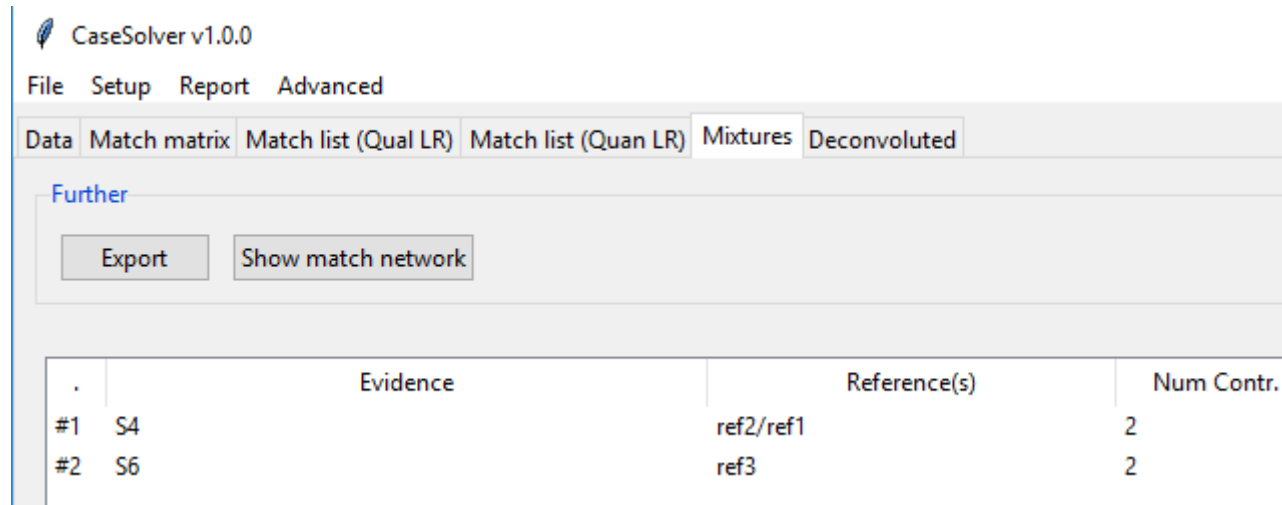
Double click on a row in Match list (Quan LR)



Mixtures

For all mixtures:

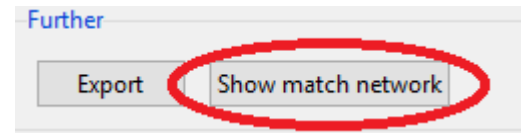
- Lists every mixture evidences.
- Candidate matches with $LR > \text{threshold}$ given in “References”
- Estimated number of contributors also given.
- Can be exported.
- List can also be viewed before “comparison”.



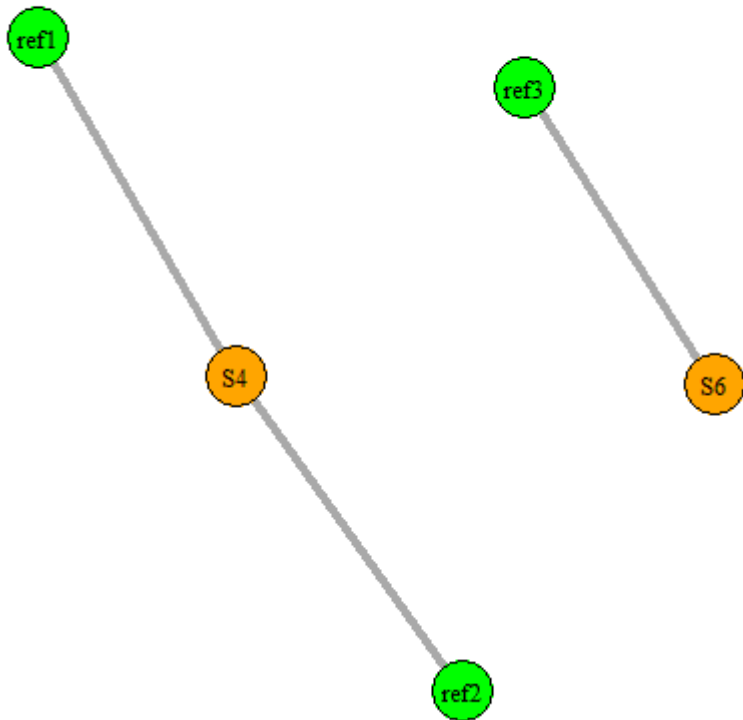
The screenshot shows the CaseSolver v1.0.0 application window. The 'Mixtures' tab is selected in the top navigation bar. Below the navigation bar, there are two buttons: 'Export' and 'Show match network'. The main area displays a table with the following data:

	Evidence	Reference(s)	Num Contr.
#1	S4	ref2/ref1	2
#2	S6	ref3	2

Show match candidates



Matches for CaseESX



A match network given:

- The width of the edge is proportional with LR

Traffic lights on profiles:

- **Green**: References
- **Orange**: 2-person mixtures
- **Red**: at least 3-person mixtures

Further evaluation*

Double click on row for further evaluation

The screenshot shows the CaseSolver v1.0.0 application window. The 'Further' tab is active, displaying a table with two rows. The first row is highlighted in blue. A dialog box titled 'Deconvolution/Show expected peak heights' is open, showing the 'Evidence=' field set to 'S4', 'Number of contributors=' set to '2', and 'Condition on:' with checkboxes for 'ref2' and 'ref1' both checked. A 'Calculate' button is at the bottom of the dialog. An arrow points from the text '*evaluation here is' to the 'Calculate' button.

	Evidence	Reference(s)	Num Contr.
#1	S4	ref2/ref1	2
#2	S6	ref3	2

Deconvolution/Show expected peak heights

Evidence= S4

Number of contributors= 2

Condition on: ☒ ref2 ☒ ref1

Calculate

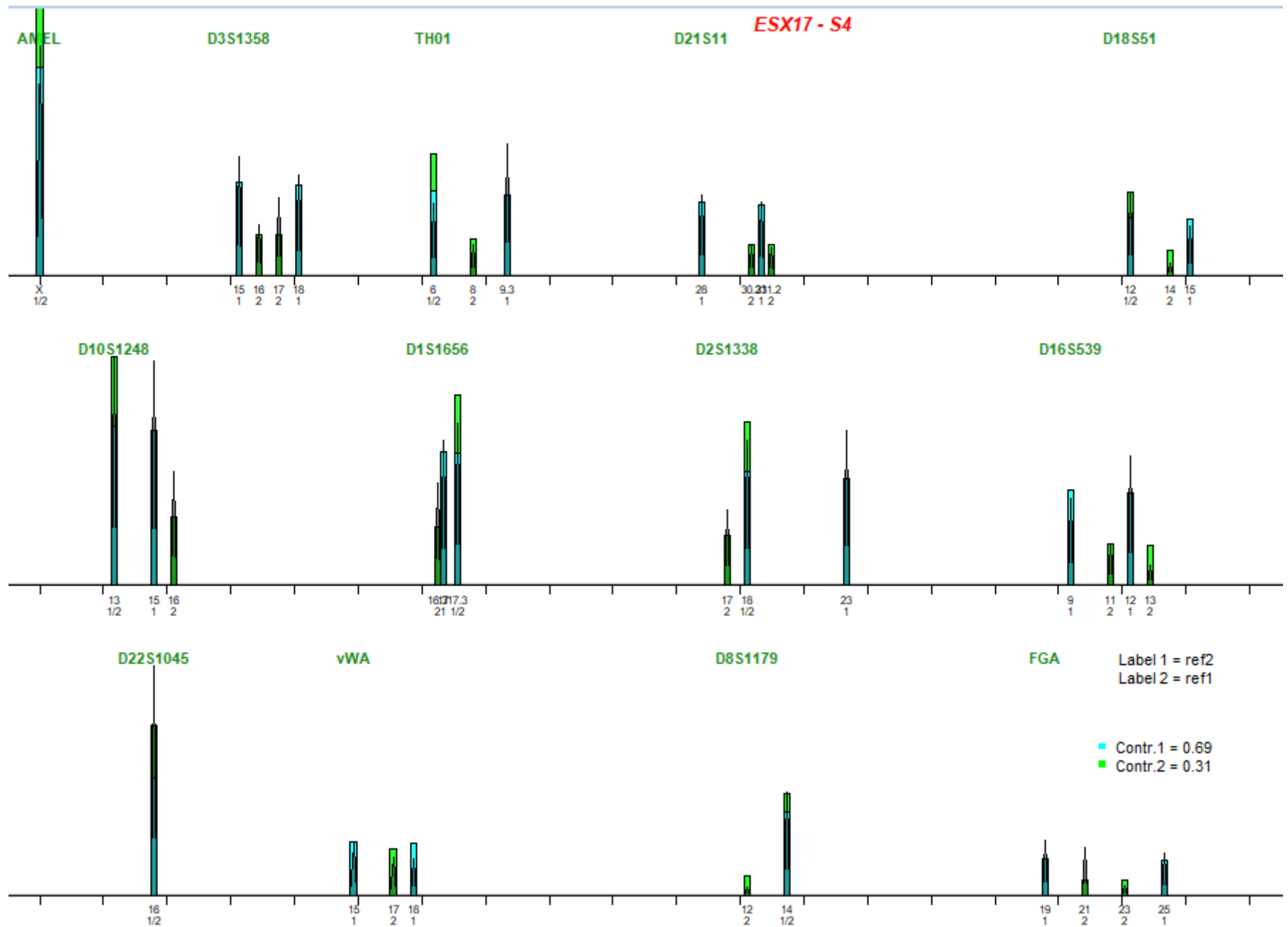
Specify your hypothesis:

- Number of contributors
- Conditional references

*evaluation here is

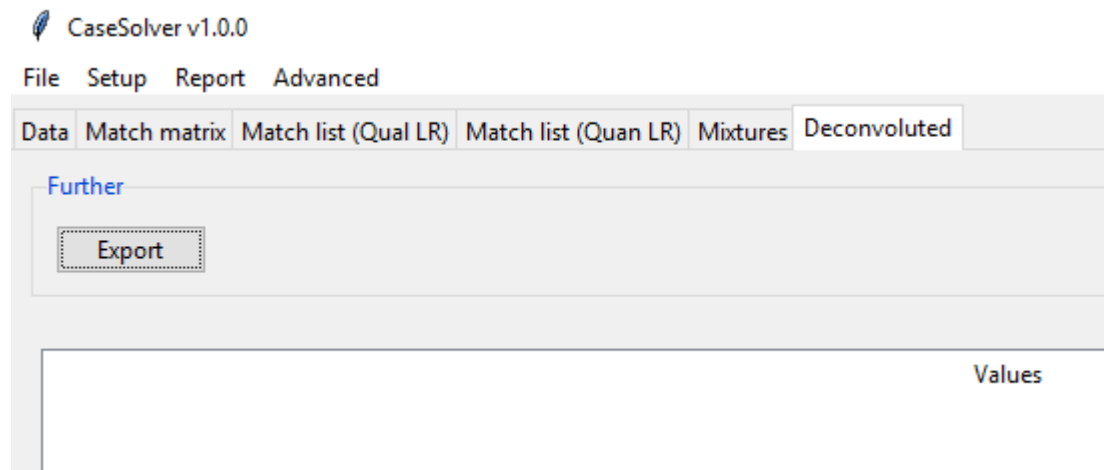
- 1) Show “model fitted/expected peak heights”
- 2) Deconvolve unknown contributors

Model fitted peak heights



Deconvolution results

Genotypes of unknown contributor(s) are automatically deduced* and presented as candidate(s) in "Deconvoluted" table.



No candidates found.

*Deduction requires that $\text{Pr}(1. \text{ Top geno}) / \text{Pr}(2. \text{ Top geno}) > \text{threshold}$
Also possible: Single deduced allele if $\text{Pr}(\text{allele}) > 0.99$

Deducing the unknown in S6

CaseSolver v1.0.0

File Setup Report Advanced

Data Match matrix Match list (Qual LR) Match list (Quan LR) Mixtures Deconvoluted

Further

Export Show match network

	Evidence	Reference(s)	Num Contr.
#1	S4	ref2/ref1	2
#2	S6	ref3	2

Deconvolution/Show expected peak heights

Evidence= S6

Number of contributors= 2

Condition on: ☒ ref3

Calculate

CaseSolver v1.0.0

File Setup Report Advanced

Data Match matrix Match list (Qual LR) Match list (Quan LR) Mixtures Deconvoluted

Further

Export

	Component	Conditional	nC	MixProp	D3S1358	TH01	D21S11	D18S51	D10S124	D1S1656	D2S1338	D16S539	D22S1045	VWA	D8S1179	FG
#1	S6-C2	ref3	2	0.34	14/15	9.3	30/31.2	17/20	14/16	13/16.3	18/26	10	16	17/18	10/11	22/2

Gives conditional references

Estimated mixture proportion for deduced component

2. allele unsure

Confirm deduced component

”Double-click” a candidate component

CaseSolver v1.0.0

File Setup Report Advanced

Data Match matrix Match list (Qual LR) Match list (Quan LR) Mixtures Deconvoluted

Further

Export

	Component	Conditional	nC	MixProp	D3S1358	TH01	D21S11	D18S51	D10S124	D1S1656	D2S1338	D16S539	D22S1045	VWA	D8S1179	FGA
#1	S6-C2	ref3	2	0.34	14/15	9.3	30/31.2	17/20	14/16	13/16.3	18/26	10	16	17/18	10/11	22/23

Confirm

Do you want to add the deconvoluted profile S6-C2 to the references?

Yes No

Edit or add new reference profiles

Sample ID	AMEL	D3S1358	TH01	D21S11	D18S51	D10S1248	D1S1656	D2S1338	D16S539	D22S1045	VWA	D8S1179	FGA	D2S441
ref1	X/X	16/17	6/8	30.2/31.2	12/14	13/16	16.3/17.3	17/18	11/13	16/16	17/17	12/14	21/23	11/12
ref2	X/X	15/18	6/9.3	28/31	12/15	13/15	17/17.3	18/23	9/12	16/16	15/18	14/14	19/25	11/14
ref3	X/Y	16/18	6/8	28/28	14/16	15/16	10/17.3	16/18	11/12	15/16	17/17	12/14	24/25	10/10
Unknown 1	X/Y	16/18	6/7	30/31.2	14/14	13/16	12/15	20/23	9/11	15/17	14/17	13/14	23/23	10/10
S6-C2		14/15	9.3	30/31.2	17/20	14/16	13/16.3	18/26	10	16	17/18	10/11	22/23	11/11

Save profile

User can edit:

- SampleID name
- Alleles

Added deconvolved component

The deduced component is added to references.

CaseSolver v1.0.0

File Setup Report Advanced

Data Match matrix Match list (Qual LR) Match list (Quan LR) Mixtures Deconvoluted

Select Case ID

CaseESX Import

☒ Sort Evids by # ☐ Sort Evids by Sample.ID ☒ Sort Refs by # ☐ Sort Refs by Sample.ID

Evidence(s) Reference(s)

ID	Sam	MatchStat	AMt	D3S1358	TH01	D21S11	D18S51	D10S124	D1S1656
#1	S3	Unknown	X/Y	16/18	6/7	30/31.2	14	13/16	12/15
#2	S5	ref3	X/Y	16/18	6/8	28	14/16	15/16	10/17.3
#3	S1	ref2	X	15/18	6/9.3	28/31	12/15	13/15	17/17.3
#4	S2	ref1	X	16/17	6/8	30.2/31.2	12/14	13/16	16.3/17.3
#5	S4	mixture	X	15/16/17/18	6/8/9.3	28/30.2/31/31.2	12/14/15	13/15/16	16.3/17/17.3
#6	S6	mixture	X/Y	14/15/16/18	6/8/9.3	28/30/31.2	14/16/17/20	14/15/16	10/13/16.3/17.3

ID	SampleNa	AMt	D3S1358	TH01	D21S11	D18S51	D10S12	D1S1656	D2S1338	D16S	D22S	VWA
#1	ref1	X/X	16/17	6/8	30.2/31.2	12/14	13/16	16.3/17.3	17/18	11/13	16/16	17/17
#2	ref2	X/X	15/18	6/9.3	28/31	12/15	13/15	17/17.3	18/23	9/12	16/16	15/18
#3	ref3	X/Y	16/18	6/8	28/28	14/16	15/16	10/17.3	16/18	11/12	15/16	17/17
#4	Unknown	X/Y	16/18	6/7	30/31.2	14/14	13/16	12/15	20/23	9/11	15/17	14/17
#5	S6-C2		14/15	9.3	30/31.2	17/20	14/16	13/16.3	18/26	10	16	17/18

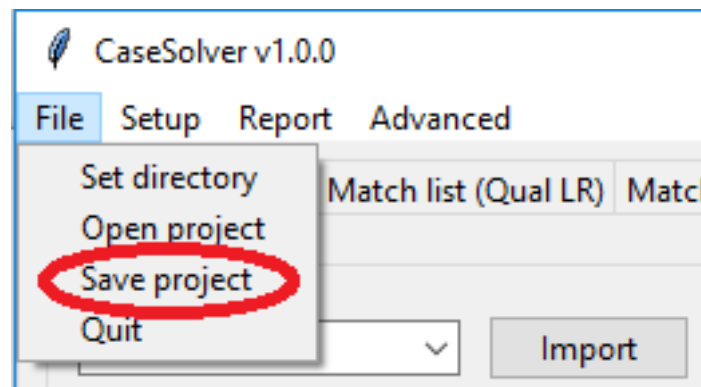
CaseSolver supports that a reference only have one allele.

Run "Calculate IBS" to check if the deduced ref. is similar to any others.

Save/Load project

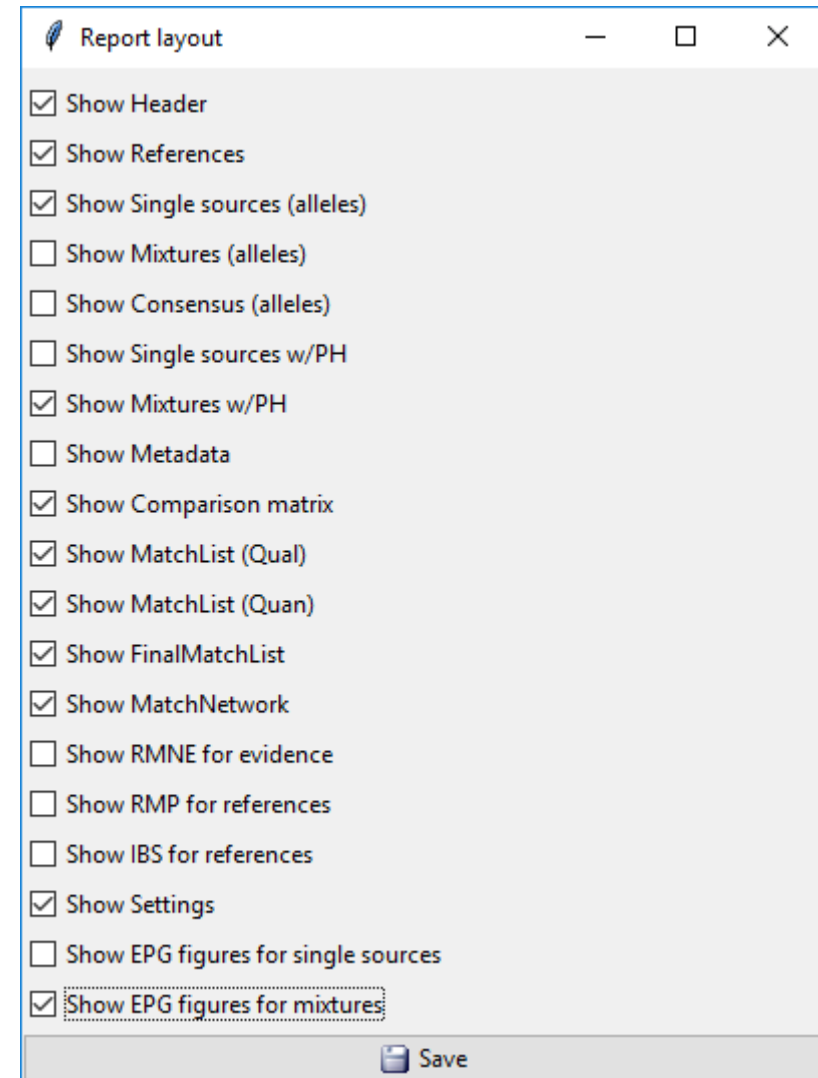
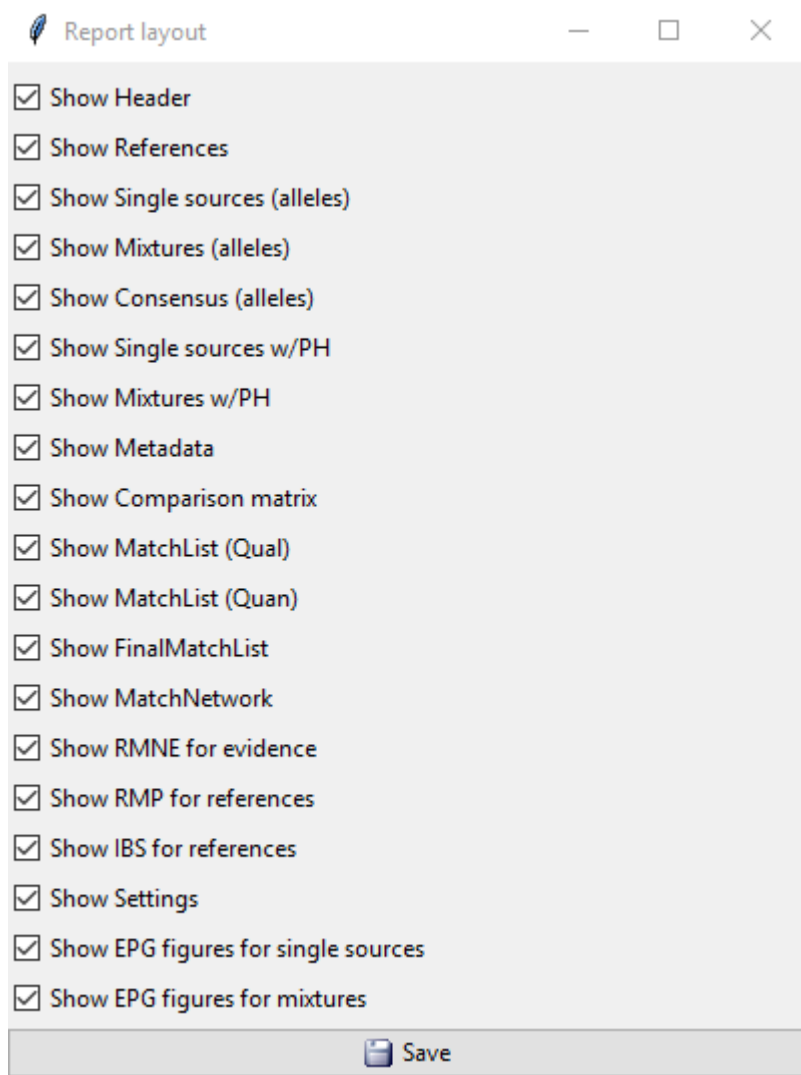
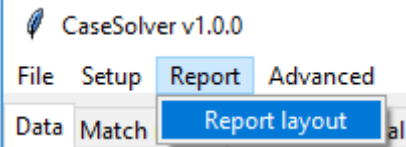
Useful to **save** project once all comparisons/analysis are done

Restore a project by **open** project (at any time)



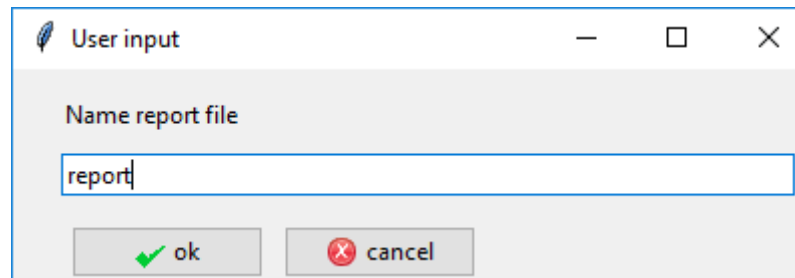
Report

Select what to include



Create Report

(click at any time during usage)
Directly opens the default browser



A screenshot of a 'User input' dialog box. The dialog has a title bar with a feather icon, the text 'User input', and standard window controls (minimize, maximize, close). The main area is light gray and contains the label 'Name report file' above a text input field. The input field contains the text 'report'. At the bottom, there are two buttons: 'ok' with a green checkmark icon and 'cancel' with a red 'X' icon.

User input

Name report file

report

ok cancel

Report for Case CaseESX

CaseSolver version 1.0.0 (euroformix_1.11.4).

R version 3.5.0 (2018-04-23)

User: oyvbl

Created: 2018-06-28 14:14:08

References

	SampleName	AMEL	D3S1358	TH01	D21S11	D18S51	D10S1248	D1S1656	D2S1338	D16S539	D22S1045	VWA	D8S1179	FGA	D2S441	D12S391	D19S433	SE33
1	ref1	X/X	16/17	6/8	30.2/31.2	12/14	13/16	16.3/17.3	17/18	11/13	16/16	17/17	12/14	21/23	11/12	20/22	13/16	19/34
2	ref2	X/X	15/18	6/9.3	28/31	12/15	13/15	17/17.3	18/23	9/12	16/16	15/18	14/14	19/25	11/14	15/21	13/13	29.2/31.2
3	ref3	X/Y	16/18	6/8	28/28	14/16	15/16	10/17.3	16/18	11/12	15/16	17/17	12/14	24/25	10/10	18/24	13/13	17/27.2
4	Unknown 1	X/Y	16/18	6/7	30/31.2	14/14	13/16	12/15	20/23	9/11	15/17	14/17	13/14	23/23	10/10	18/25	14/14	19/19
5	S6-C2		14/15	9.3	30/31.2	17/20	14/16	13/16.3	18/26	10	16	17/18	10/11	22/23	11/11	23	13/15.2	22.1/28.2

Single source profiles

	SampleName	MatchStatus	AMEL	D3S1358	TH01	D21S11	D18S51	D10S1248	D1S1656	D2S1338	D16S539	D22S1045	VWA	D8S1179	FGA	D2S441	D12S391	D19S433	SE33
1	S3	Unknown 1	X/Y	16/18	6/7	30/31.2	14	13/16	12/15	20/23	11/9	15/17	14/17	13/14	23	10	18/25	14	19
2	S5	ref3	X/Y	16/18	6/8	28	14/16	15/16	10/17.3	16/18	11/12	15/16	17	12/14	24/25	10	18/24	13	17/27.2
3	S1	ref2	X	15/18	6/9.3	28/31	12/15	13/15	17/17.3	18/23	12/9	16	15/18	14	19/25	11/14	15/21	13	29.2/31.2
4	S2	ref1	X	16/17	6/8	30.2/31.2	12/14	13/16	16.3/17.3	17/18	11/13	16	17	12/14	21/23	11/12	20/22	13/16	19/34

Mixtures w/peak heights

S4

	AMEL	D3S1358	TH01	D21S11	D18S51	D10S1248	D1S1656	D2S1338	D16S539	D22S1045	VWA	D8S1179	FGA	D2S441	D12S391	D19S433	SE33
1	X (8892)	15 (4614)	6 (2775)	28 (3139)	12 (3248)	13 (5577)	16.3 (2484)	17 (1832)	9 (2122)	16 (14730)	15 (3363)	12 (465)	19 (3563)	11 (2711)	15 (3246)	13 (6211)	19 (1609)
2		16 (1953)	8 (1203)	30.2 (1119)	14 (493)	15 (5468)	17 (3545)	18 (3532)	11 (1011)		17 (2470)	14 (6654)	21 (3087)	12 (1806)	20 (782)	16 (299)	29.2 (742)
3		17 (3027)	9.3 (5086)	31 (2846)	15 (1931)	16 (2767)	17.3 (3949)	23 (3777)	12 (3154)		18 (2372)		23 (560)	14 (3300)	21 (2216)		31.2 (1014)
4		18 (3892)		31.2 (1065)				13 (477)					25 (2743)		22 (1286)		34 (569)

Comparisons

Comparison matrix

	SampleName	S4	S6
1	ref1	1	
2	ref2	1	
3	ref3		1
4	Unknown 1		

Match list (Qual LR)

	Evidence	Reference	MAC	log10LR	numContr
1	S4	ref1	1	14.58	2
2	S6	ref3	1	13.65	2
3	S4	ref2	1	13.43	2

Match list (Quan LR)

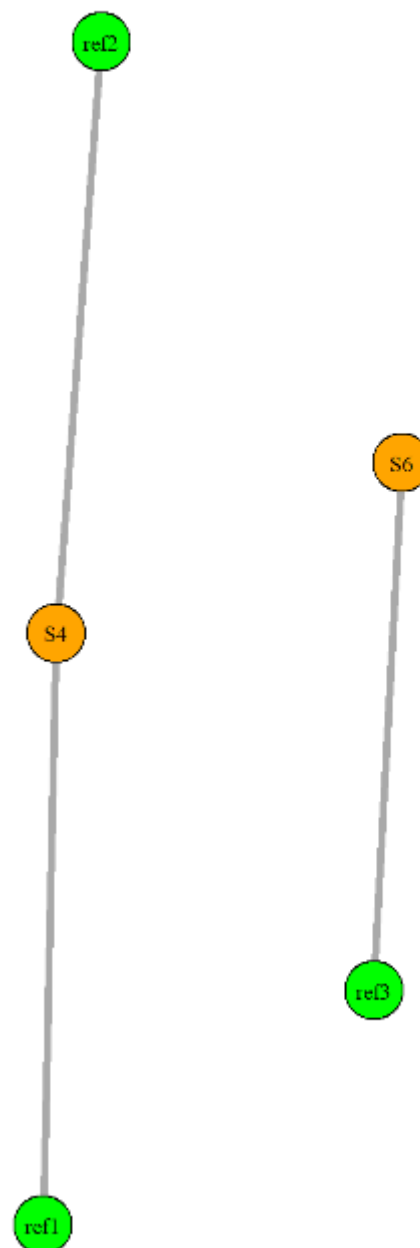
	Evidence	Reference	MAC	log10LR	numContr
1	S4	ref2	1	20.16	2
2	S6	ref3	1	19.01	2
3	S4	ref1	1	18.73	2

Final match list (w/all mixtures)

	Evidence	Reference(s)	Num Contr.
1	S4	ref2/ref1	2
2	S6	ref3	2

Match network

Matches for CaseESX



Settings:

Thresholds:

MAC threshold=0.9

Qual. LR threshold=10

Quan. LR threshold=1000

Minimum loci=7

Deconv.ratio=10

Deconv.alleleProb=0.99

Model:

Frequency file=C:/Users/oyvbl/Desktop/tutorialdata/ESX17_Norway.csv

Qualitative (LRmix):

Drop-in prob=0.05

Quantitative (EuroForMix):

Detection threshold=50

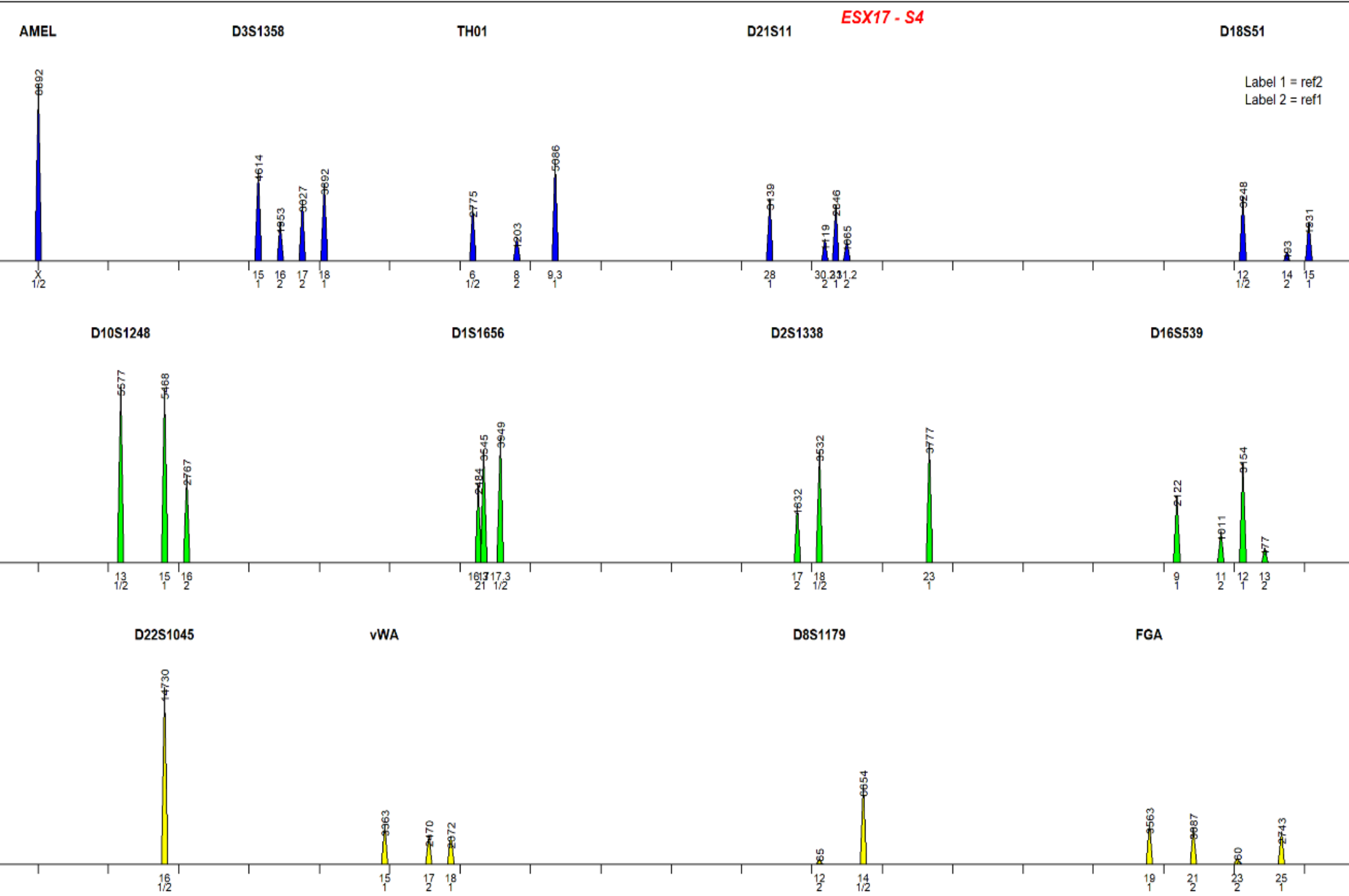
Kit=ESX17

Degradation model=ON

Stutter model=OFF

Drop-in prob=0.05

Mixture profiles



Other functionalities

Functionalities

Compare

Create Report

Add reference profile

Export profile(s)

Calculate RMP

Calculate IBS

Restart

1

2

3

4

3

Random match probability calculations

Evidence(s)

Reference(s)

ID	SampleName	RMNE
#1	S1	2.71e-23
#2	S3	8.35e-27
#3	S4	2.96e-23
#4	S5	8.72e-16
#5	S2	1.23e-15
#6	S6	1.87e-15

ID	SampleName	RMP
#1	ref1	2.26e-32
#2	ref2	2.55e-32
#3	ref3	1.26e-31
#4	Unknown 1	6.84e-32
#5	Unknown 2	3.28e-32

Note: Inserting minimum allele freq of 0.001 if not seen.

1

Edit or add new reference profiles

Sample ID	AMEL	D3S1358	D1S1656	D2S441	D10S1248	D13S317	PENTA E	D16S539	D18S51	D2S1338	CS
ref1	X/X	16/17	17/18.3	10/15	13/14	12/9	12/16	11/11	12/15	17/19	10/
ref2	X/Y	15/18	15/16	14/14	13/15	12/13	15/5	10/11	15/15	20/24	10/
ref3	X/X	16/18	15.3/17	14/14	13/14	12/14	18/9	10/9	13/14	17/20	10/
Unknown 1	X/X	14/17	12/17.3	10/16	13/14	11/12	10/15	12/9	12/18	16/25	10/
Unknown 2	X/Y	16/16	15/17.3	14/14	13/15	12/12	13/17	11/12	15/17	20/23	11/
Name	A/B	A/B	A/B	A/B	A/B	A/B	A/B	A/B	A/B	A/B	A/I

Save profile

4

Similarity of references

Comparisons

IBS	Comparison
20	S4-C1 - ref3
19	ref3 - ref1
19	Unknown 1 - ref1
18	S4-C1 - Unknown 1
18	S4-C1 - Unknown 2
17	S4-C1 - ref1
17	ref3 - ref2
17	Unknown 1 - ref3
16	Unknown 2 - ref2
14	ref2 - ref1
14	Unknown 1 - ref2

2

Export data

Open directly in software

EuroForMix

Data selection

Evidence(s) Reference(s)

- ☒ S2 ☒ ref1
☒ S6 ☒ ref2

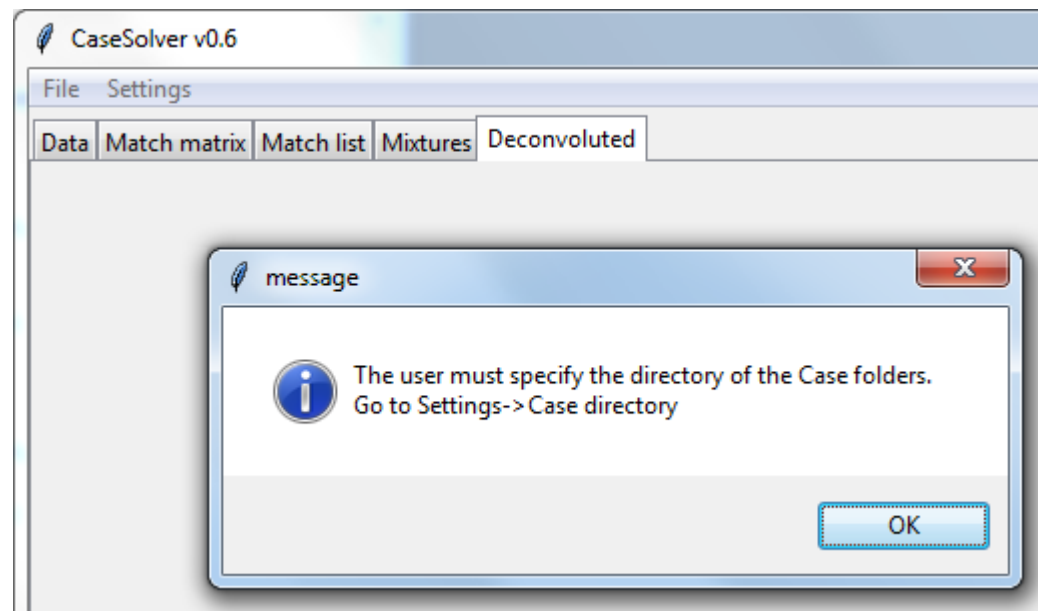
Data export

☐ Store evidence(s) ☐ Store reference(s)

☒ Export peak heights

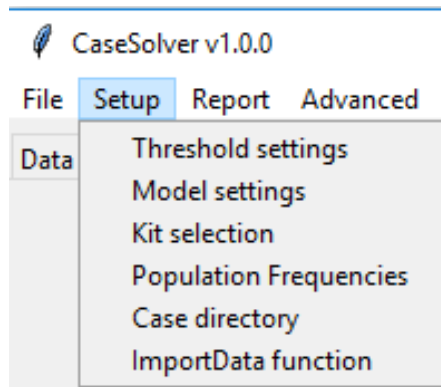
Details about

”setting up CaseSolver for the first time”



Setting up CaseSolver for the first time*

The user must specify the following:

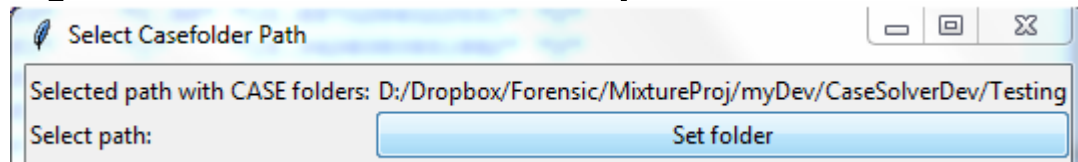
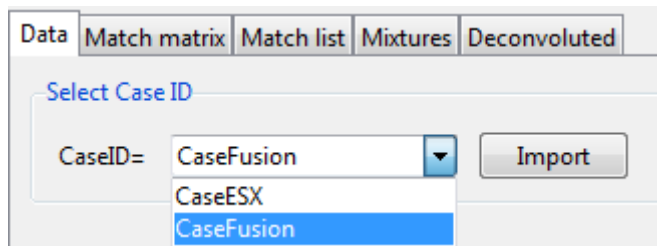
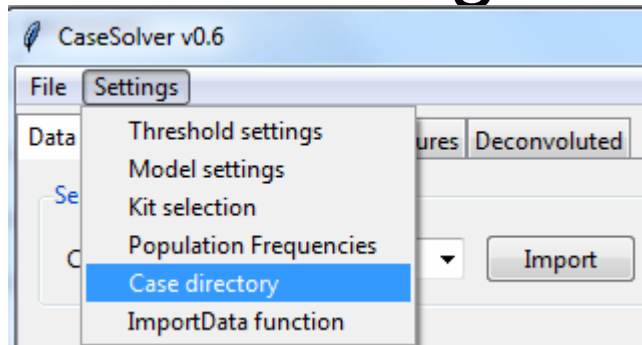


- 1) **ImportData function:** A R-script converting profiles in datafiles to “casesolver format”.
- 2) **Case directory:** A directory with case-folders (which includes datafiles).
- 3) **Population frequencies**
 - Necessary for LR calculations
- 4) **Kit selection**
 - Necessary for EPGs/LR calcs.
- 5) **Model settings**
- 6) **Threshold settings**

*Settings are stored permanently

2) Case directory:

A specified directory where a folder for each case are given (by its casename).



Selected directory includes casefolders:

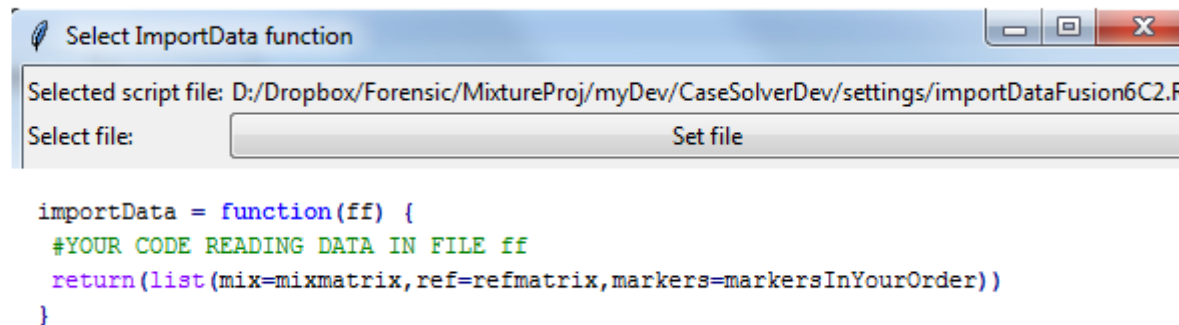
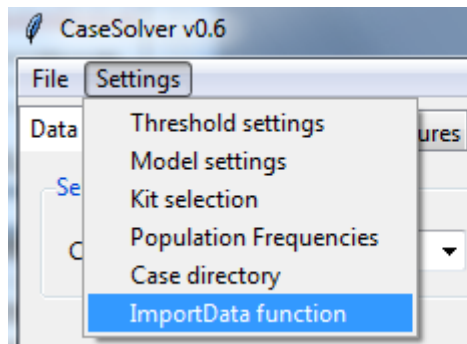
Local Disk (D:) > Dropbox > Forensic > MixtureProj > myDev > CaseSolverDev > Testing >			
Name	Date modified	Type	Size
CaseESX	12/20/2017 5:41 PM	File folder	
CaseFusion	3/4/2018 2:00 PM	File folder	

Casefolder includes data files:

Dropbox > Forensic > MixtureProj > myDev > CaseSolverDev > Testing > CaseFusion >			
Name	Date modified	Type	Size
report	3/4/2018 6:58 PM	File folder	
evids.csv	3/4/2018 1:59 PM	CSV File	7 KB
other.txt	3/5/2018 10:39 AM	Text Document	0 KB
refs.csv	3/4/2018 1:59 PM	CSV File	2 KB

- CaseSolver applies the R-function importData to every existing file in the selected CaseFolder.
- CaseSolver accepts that some files are non-data.

1) ImportData function



- Select a file which includes a R-function named "importData".
- importData MUST take one filename as parameter, read the file, and convert the data to the following output format:

The output MUST be a list with the elements "markers", "mix" and "ref":

Example of output from a file with only evidence profiles:

```
$mix  
SampleName Markers Alleles Heights  
"S1" "AMEL" "X" "2043"  
"S1" "D3S1358" "14/17" "729/1053"  
"S1" "D1S1656" "12/17.3" "613/1013"  
"S1" "D2S441" "10/16" "677/525"  
"S1" "D10S1248" "13/14" "238/559"  
"S1" "D13S317" "11/12" "824/777"  
"S1" "Penta E" "10/15" "712/645"  
  
$ref  
numeric(0)  
  
$markers  
"AMEL" "D3S1358" "D1S1656" "D2S441" "D10S1248" "D13S317" "Penta E"
```

"mix" must be a matrix with markers given per row. Allele info must be collapsed with "/"

The column order is important, but the column names are not.

The vector in "markers" will decide what markers (and the order) are presented in the GUI

1) ImportData function (continue)

Example of output from a file with only reference profiles:

```
$mix
numeric(0)

$ref
SampleName Markers Alleles
"ref1"      "AMEL"      "X/X"
"ref1"      "D3S1358"   "16/17"
"ref1"      "D1S1656"   "17/18.3"
"ref1"      "D2S441"    "10/15"
"ref1"      "D10S1248"  "13/14"
"ref1"      "D13S317"   "9/12"
"ref1"      "Penta E"   "12/16"
"ref3"      "AMEL"      "X/X"
"ref3"      "D3S1358"   "16/18"
"ref3"      "D1S1656"   "15.3/17"
"ref3"      "D2S441"    "14/14"
"ref3"      "D10S1248"  "13/14"
"ref3"      "D13S317"   "12/14"
"ref3"      "Penta E"   ""
$markers
"AMEL"      "D3S1358"   "D1S1656"   "D2S441"    "D10S1248"  "D13S317"   "Penta E"
```

Important notes for reference profiles:

- 1) "Empty markers" must be given as "".
- 2) Homozygous variants must be given as "10/10"
- 3) Single alleles like "12" is possible (like for Y-STRs variants for instance)

The 2 and 3 variants are sometimes treated differently in the program:

- See slide "Handling single allele"

1) ImportData function (optional)

An additional list element "meta" with metadata can be given in the output:

```
$meta
$meta$`Sample type`
  Sample Type
[1,] "S1"    "Blood"
[2,] "S2"    "Saliva"

$meta$`Negative samples`
  Sample Status
[1,] "S7"    "Negative"
[2,] "S8"    "Negative"
```

"meta" must contain list elements (with names given as strings) which again contains matrix elements.

The information will be presented in the generated report:

Metadata

Sample type

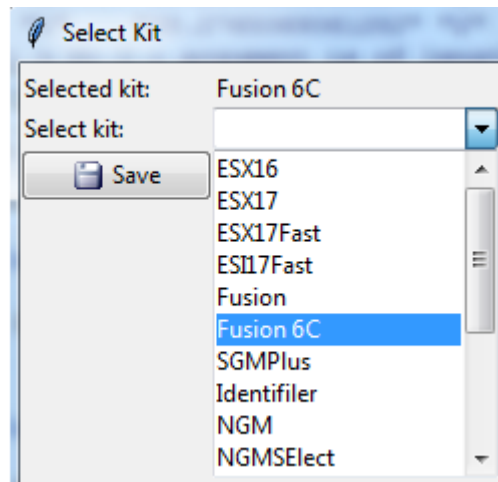
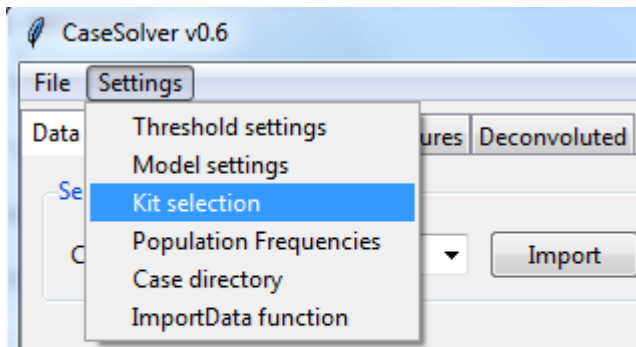
Sample	Type
S1	Blood
S2	Saliva

Negative samples

Sample	Status
S7	Negative
S8	Negative

3) Kit selection

- Necessary for
 - Showing EPGs
 - Calculating LR in comparison.

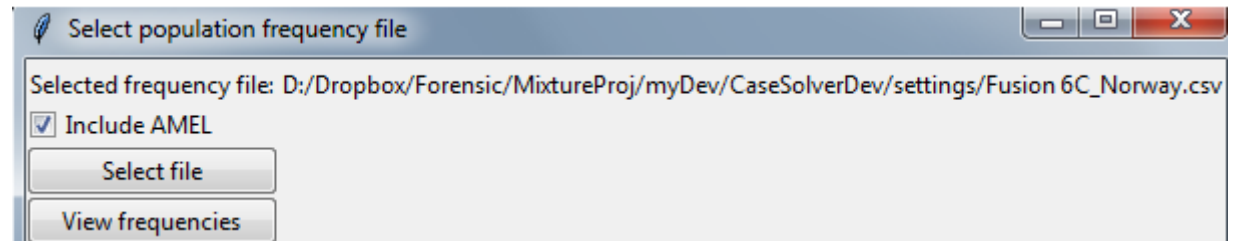
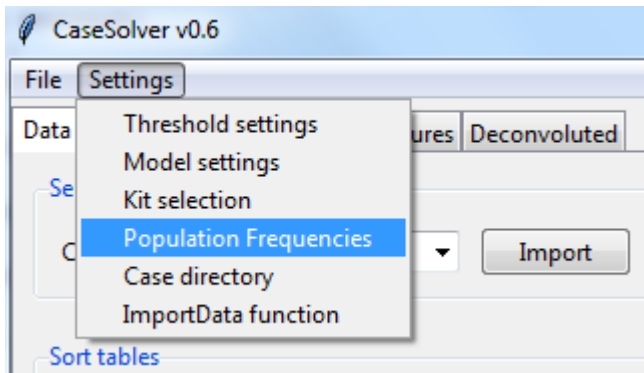


The kit-info is necessary in order for CaseSolver to get the basepair information.

- Used for showing EPGs
- Used for applying the degradation model (always on).

4) Population frequencies

- Necessary for LR, RMNE and RMP calculations
- User must select a file including allele frequencies
 - LRmix/EuroForMix format



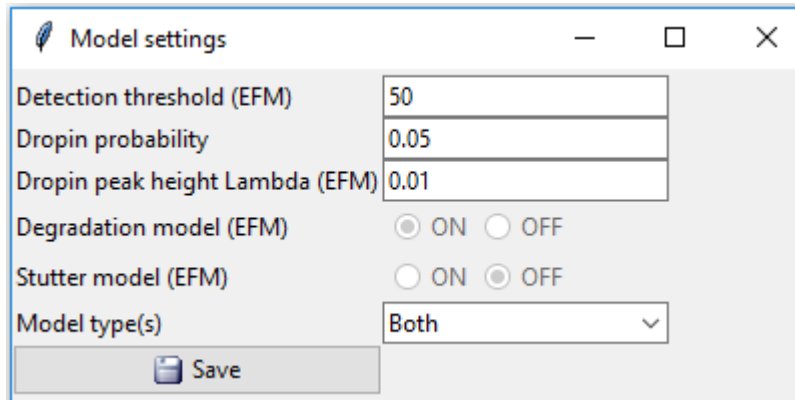
The 'Allele frequencies' window displays a table with four columns: A1, A2, A3, and A4. The table lists allele frequencies for four markers: D3S1358, D1S1656, D2S441, and D10S1248. The values are numerical, representing the frequency of each allele. The value 0.0342742076431483 in the A3 column for D10S1248 is highlighted.

Marker	A1	A2	A3	A4
D3S1358	10	11	12	13
D3S1358	5.21594105987922e-05	0.0046421909432932	5.21594105987922e-05	0.0032860406677234
D1S1656	10	11	12	13
D1S1656	0.00028801812269572	0.0740207315328316	0.132200056317224	0.0506912215944604
D2S441	8	9	9.1	10
D2S441	0.00115207038594358	0.000864055289458522	0.000288018096486062	0.194988065321002
D10S1248	10	11	12	13
D10S1248	0.00057603712845628	0.00432028096342265	0.0342742076431483	0.315956070458204

User can choose to include AMEL:
(Marker name must be AMEL)
Included: $X = 0.75$, $Y = 0.25$

This enables that the peak heights in AMEL
is utilized in the analysis.

5) Model settings



Model settings

Detection threshold (EFM) 50

Dropin probability 0.05

Dropin peak height Lambda (EFM) 0.01

Degradation model (EFM) ☒ ON ☐ OFF

Stutter model (EFM) ☐ ON ☒ OFF

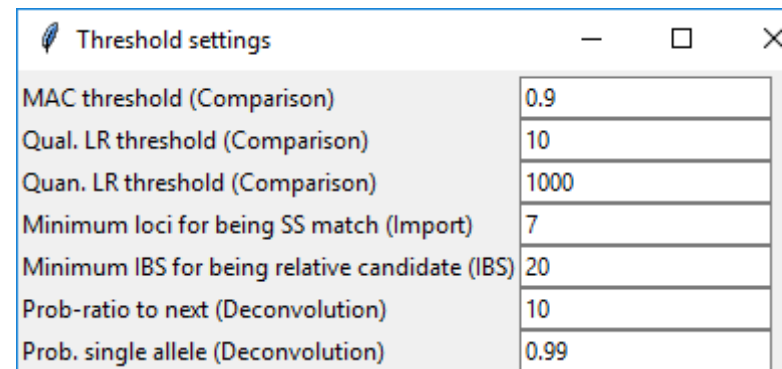
Model type(s) Both

Save

These values are settings used in the LR calculations

- **Detection threshold (EFM only):**
 - The peak height threshold used in the analysis.
- **Dropin probability:**
 - The allele dropin probability (using by both models)
- **Dropin peak height Lambda (EFM only)**
 - The parameter used to model the dropin peak heights

6) Thresholds settings



Threshold settings	
MAC threshold (Comparison)	0.9
Qual. LR threshold (Comparison)	10
Quan. LR threshold (Comparison)	1000
Minimum loci for being SS match (Import)	7
Minimum IBS for being relative candidate (IBS)	20
Prob-ratio to next (Deconvolution)	10
Prob. single allele (Deconvolution)	0.99

In Import:

- **Minimum loci for being SS match:**

- In situation of missing markers (in SingleSource-evid/ref comparison). This threshold is the required minimum compared non-missing loci.

In Comparison:

- **MAC threshold**

- The required number of proportion of alleles of a reference to be included in a compared mixture profile. All candidates above this threshold are further analysed with LR calculation.

- **LR threshold (for Qual or Quan model)**

- The required LR value for that a reference is assigned as a "match" to the compared mixture profile.

In Calculate IBS:

- **Minimum IBS for being relative candidate**

- The required number of sharing alleles between two references to be assigned as a candidate.

In Deconvolution:

- **Prob-ratio to next**

- The threshold gives how "sure" a top ranked genotype must be in order to be a deduced genotype.
 $\text{Pr}(\text{1st ranked geno})/\text{Pr}(\text{2nd ranked geno}) > \text{threshold}$

- **Prob. Single allele**

- The threshold gives how "sure" a top ranked allele must be in order to be a deduced allele.
This is in case when deducing a genotype fails.

Litterature

- Haned 2011: *Forensim: an open-source initiative for the evaluation of statistical methods in forensic genetics*
- Bleka et al. 2016: *EuroForMix: An open source software based on a continuous model to evaluate STR DNA profiles from a mixture of contributors with artefacts*
- Bleka et al. 2017: *dnamatch2: An open source software to carry out large scale database searches of mixtures using qualitative and quantitative models*