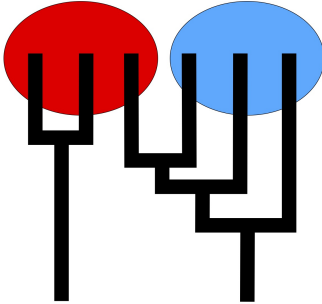


MIGRATE tutorial

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This tutorial has three sections:

0. Short overview of the program
1. How do we specify models
2. Run a model selection exercise

If you are in the course: all material is available in the folder `moledata/migrate_tutorial`

If you are not in the course: Download the necessary files from http://www.peterbeerli.com/workshops/mb1/2018/tutorial_material.zip and unpack the *tutorial_material.zip* file; you have now a directory *migrate_tutorial*

Or you can use *wget* to download the package directly to your home directory using this command:

```
wget http://www.peterbeerli.com/workshops/mb1/2018/tutorial_material.zip
unzip tutorial_material.zip
cd migrate_tutorial
```

Overview of the program

[*first 30 minutes*]

migrate is a Bayesian population genetics inference program that is based on the structured coalescence. It uses DNA/RNA sequence data or microsatellite data. It can run on computer clusters (using parallel software tools based on the MPI standard). It is distributed as Opensource (MIT license) from Migrate's main website.

migrate can estimate parameters, such as population sizes, immigration rates, and divergence times of fairly complex models. Originally, it was a pure population genetics program, but with the introduction of divergence, it can handle closely related species, admixed populations, including potential hybrids as long as your data include multiple individuals of the same group. This tutorial will introduce you to these models.

Efficient running on your system

migrate is distributed in source code and binaries for Mac and Windows computers. To run **migrate** efficiently on Linux clusters compile it yourself using the MPI libraries openmpi or mvapich2. The Windows binary can run on Windows 7-11, although it may not be the most efficient way to run the program. If you have multiple loci and a computer with multiple cores (> 4) use the parallel version.

Menu and starting the program

migrate uses a menu to operate. The menu can save all options into a file which is called by default *parmfile*. The parmfile is a textfile that can be edited with a text editor; all lines starting with a # are comments and try to explain the options. You can write your own comments into the parmfile, but these will be overwritten when the *parmfile* is saved again through the menu. Starting the program can be done like this

```
migrate-n
migrate-n parmfile
migrate-n parmfile -nomenu
migrate-n -version
migrate-n -help
```

If the program is started without the *-nomenu* option it displays the main menu

```
+++++
+                                     +
+  POPULATION SIZE, MIGRATION, DIVERGENCE, ASSIGNMENT, HISTORY  +
+  Bayesian inference using the structured coalescent            +
+                                     +
+++++
```

```
PDF output enabled [Letter-size]
Version 5.0(git:v5.0-30-g634f887)  [March-20-2021]
Program started at   Tue Oct 26 09:14:24 2021
```

```
=====
MAIN MENU
=====
```

```
D      Data type currently set to: DNA sequence model
I      Input/Output formats and Event reporting
P      Parameters  [start, migration model]
S      Search strategy
W      Write a parmfile
Q      Quit the program
```

To change the settings type the letter for the menu to change
Start the program with typing Yes or Y

==>

Each submenu will handle options concerning Data, Run parameters, and Population model among other things.

Running

The MPI version is printing out less information than the single computer version, here an example of a log while running:

```
23:38:13 Burn-in of 200000 steps (Locus: 1/2, Replicate: 1/5)
23:38:15 Burn-in complete in 22 seconds
23:39:00 Sampling of 100000 steps (Locus: 1/2, Replicate: 1/5)
23:39:15 Sampling complete in 181 seconds
23:39:33 Sampling: prognosed end of run is 23:55 July 08 2016 [0.077777 done])
Parameter      Acceptance Current      PropWindow AutoCorr ESS
-----
Theta_1         0.085         0.00008         0.016      0.520     211.18
Theta_2         0.110         0.00211         0.024      0.515     214.11
M_2->1         0.759         982.58556        85.061      0.956      15.08
Genealogies     0.100        -3210.29272         ---         0.781      82.36
```

Output

The output will be printed into two files that are called by default *outfile* and *outfile.pdf* (the name can be changed through the menu). There is an example *outfile.pdf* here.

How do we specify models

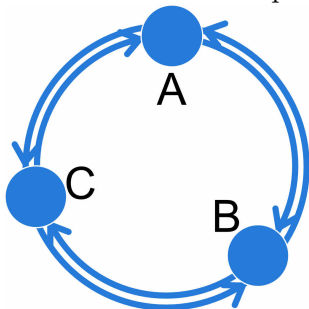
[*about 15 minutes*]

migrate uses an adjacency matrix to define the interactions among populations.

Defaults

The defaults in **migrate** are to estimate all population sizes Θ and all immigration rates M independently.

For example a 3-population model where all populations A, B, and C exchange migrants at individual rates can be specified like this:



	A	B	C
A	x	x	x
B	x	x	x
C	x	x	x

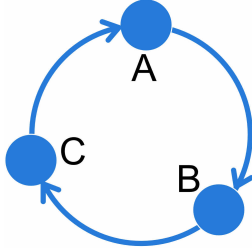
Of course, this is not all that informative, but it is the default.

Specifying models without divergence

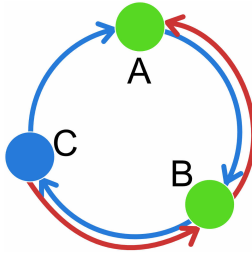
There are many ways to specify different structured models, **migrate** has a set of options to help with that:

- x or '*' means that this parameter is estimated
- 0 means that this parameter is not estimated (works only on off-diagonal elements)
- s means the migration parameter is symmetric, this implies that $M_{1 \rightarrow 2} = M_{2 \rightarrow 1}$
- c means that the value is constant and not estimated, the values needs to be specified in the the start-parameter option
- m means take the average of all parameters labeled m, Θ and M will be treated separately. A matrix full of m will be a two-parameter model (all populations share the same values for 1 Θ and 1 M).
- there are upper case variants for s and m (S, M) that use instead of the migration parameter M the number of immigrants Nm . In most cases this is not a good choice because Θ and Nm are more strongly correlated than Θ and M .
- all other lower alphabet letters except c, d, t, m, s, and x can be used to form groups of parameters (similar to m but more flexible), see example.

More examples:



	A	B	C
A	x	0	x
B	x	x	0
C	0	x	x



	A	B	C
A	e	b	a
B	a	e	b
C	0	a	x

REMINDER: the populations specified on the row of the adjacency matrix are the receiving populations; populations on the columns are the sending populations; thus in the circular unidirectional stepping stone example above, population A receives migrants from population C and we estimate the parameter $M_{C \rightarrow A}$, population B receives migrants from population A and we estimate $M_{A \rightarrow B}$ etc.

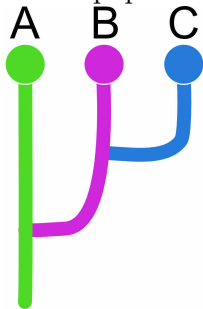
Answer these questions

Click on the question to reveal the answer, but write down the answer before you peek :-).

1. specify the matrix for a 2-population system with unidirectional migration from 2 $\rightarrow$ 1
2. specify a migration matrix for a 5-population system where population 1 and 5 are on a mainland, population 2 is an island close to 1, population 4 is close to 5, and population 3 is far out in the sea but closest to 2. ‘Close’ means reachable by rafting, and once on an island, it will be difficult to get off again.

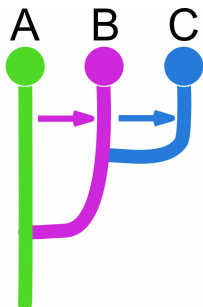
Specifying models with divergence

For the divergence specification, we also use the adjacency matrix. For example, if we have a model where the populations do not exchange migrants, we could specify the matrix like this



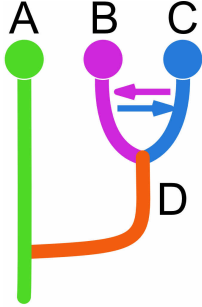
	A	B	C
A	x	0	0
B	d	x	0
C	0	d	x

- d means divergence from the ancestral column population
- D means divergence from the ancestral column population with ongoing immigration
- t means divergence time is the same for all the matrix elements with the t.



	A	B	C
A	x	0	0
B	D	x	0
C	0	D	x

Migration is problematic, and models with immigration and divergence may need additional ancestral populations to allow the estimation to be identifiable. Here is an example that needs ancestral population to get better estimates of divergence and migration.

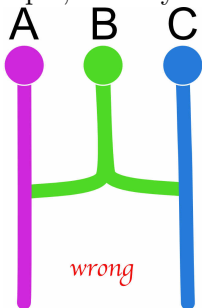


	A	B	C	D
A	x	0	0	0
B	0	x	x	t
C	0	x	x	t
D	d	0	0	x

migrate has a menu to enter this adjacency matrix, but given the many options, it may seem easier for complex scenarios to edit the parameter file (it is a text file) directly. The option is named *custom-migration* and contains the adjacency matrix, for example, the example from above looks like this

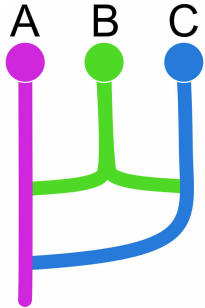
```
custom-migration={ x000 0xxt 0xxt d00x}
```

If a diagonal element is set to zero, the program will crash! There are also models that will not work well or fail. All models essentially need to be able to end in one common ancestor; for example, we may be tempted to code an admixture example like this



	A	B	C
A	x	0	0
B	d	x	d
C	0	0	x

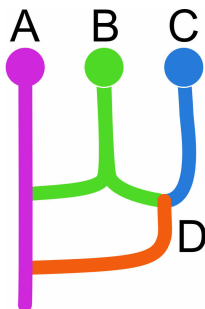
but this will not work well because we force **to have two roots**, and this can lead to failures during the run, and one can code this better as this (a) or this (b)



(a)

	A	B	C
A	x	0	0
B	d	x	d
C	d	0	x

More complicated than (a) is this (b) model that forces a sequence of divergences. Both models should deliver similar values so, although (b) will estimate population size for population D.



(b)

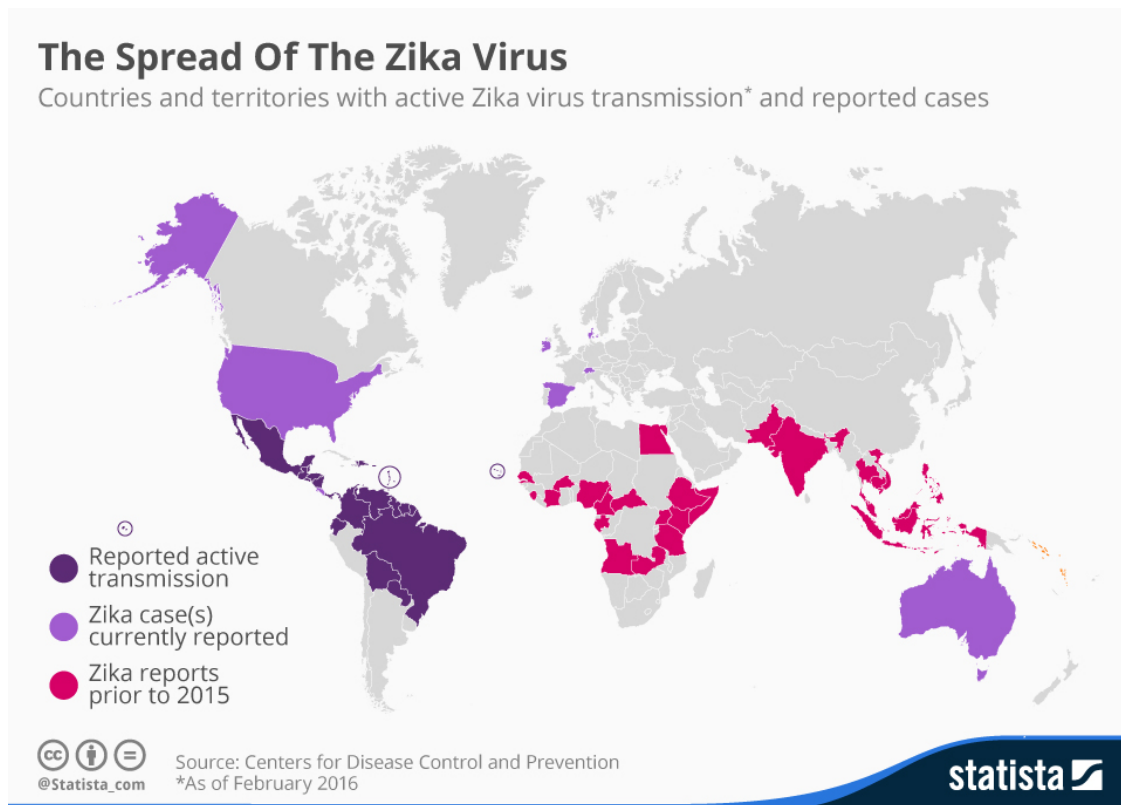
	A	B	C	D
A	x	0	0	0
B	d	x	d	0
C	0	0	x	d
D	d	0	0	x

Answer these questions

1. specify the matrix for two current populations A, B that share a common ancestor C

Run a model selection exercise

[*about 1.5 hours*] We use a real dataset of the zika virus, the data was gathered from the VIPR database. The localities include Africa, China, Brazil, Panama, Guatemala, Mexico, and Puerto Rico. There are only few sequences in some of the populations so they will be pooled in our analysis. To simplify we pool Panama, Guatemala, Mexico, and Puerto Rico into a population labeled 'Mexico'. The general consensus about the spread of zika is from Africa to Asia to the Americas. They mainly used incidence data to come to that conclusion. Here we use complete genomic data of the viruses to select among models that represent alternative hypotheses.



to the east and north Zika spread from Africa → Asia → Brazil → Mexico

to the east and north with migration Zika spread from Africa → Asia → Brazil → Mexico with recurrent migration from the source after the population split

panmictic The spread of Zika so fast and ubiquitous that we can treat Zika as a single panmictic population

to the west Zika spread from Africa → Asia and independently from Africa → Brazil → Mexico

migration Zika follows an *n-island model*

to the east and splam Zika spread from Africa → Asia → Americas (and we treat all new world locations as a panmictic unit).

twoways The population in the Americas is a 'hybrid' from Africa and Asia.

1. Your own model

For each of the models you will need to edit a parmfile. I suggest that you follow the naming schemes in this tutorial.

There is a *parmfile.template* that specifies model 1 [**to the east and north**]. Use this template to form all the other models, for each these new models you will need to do the following steps:

1. copy the *parmfile.template* to a new parmfile
2. check and fix the population relabel option
3. and/or check the custom-migration option

Model 1 to the east and north

```
cp parmfile.template parmfile_eastnorth
perl -p -i -e 's/template/eastnorth/g;' parmfile_eastnorth
# the parmfile_eastnorth does not need any editing! then execute
migrate-n parmfile_eastnorth -nomenu
```

For all other models you will use the same approach to change the template and generate the specific models. If you follow the instructions to the dot then all files will be set up correctly, if you insist on doing this by hand, you almost certainly will overwrite things and also use incorrect options.

Model 2 to the east and north with migration

```
cp parmfile.template parmfile_eastnorthmig
perl -p -i -e 's/template/eastnorthmig/g;' parmfile_eastnorthmig
<edit the parmfile_eastnorthmig: see instructions below>
migrate-n parmfile_eastnorthmig -nomenu
```

the parmfile needs to have a different *custom-migration* setting, search for the option, the current setting that does not include migration, edit it accordingly (using the example in the beginning of the tutorial, but recognize that we have a total of 4 population now, not three.

Once you have edited your copy compare with this.

Model 3 panmictic

```
cp parmfile.template parmfile_panmictic
perl -p -i -e 's/template/panmictic/g;' parmfile_panmictic
<edit the parmfile_panmictic, see below!>
migrate-n parmfile_panmictic -nomenu
```

In your editor search for the option **population-relabel** it should look like this

```
# MBL tutorial dataset zika
# in the data file the order of the population is this:
# Africa
# Asia
# Brazil
# Mexico
# Puerto Rico
#
#   population-relabel={assignment for each location in the infile}
#   example is population-relabel={1 2 2}
#
population-relabel={1, 2, 3, 4, 4}
#
```

For model 3 you need to reset to model to a single population, edit the option.
Once you have edited your copy compare with this.

Model 4 to the west

```
cp parmfile.template parmfile_west
perl -p -i -e 's/template/west/g;' parmfile_west
<edit the parmfile_west>
migrate-n parmfile_west -nomenu
```

the parmfile needs to have a different *custom-migration* setting, adjust it so that we have population splits like this Africa → Asia, Africa → Brazil → 'Mexico'.

Once you have edited your copy compare with this.

Model 5 migration only (and not divergence)

```
cp parmfile.template parmfile_migration
perl -p -i -e 's/template/migration/g;' parmfile_migration
<edit the parmfile_migration>
migrate-n parmfile_migration -nomenu
```

the parmfile needs to have a different *custom-migration* setting, adjust to the *n-island* model with migration among all [!] populations

Once you edited your copy compare with this.

Model 6 to the east and splam

```
cp parmfile.template parmfile_eastsplam
perl -p -i -e 's/template/eastsplam/g;' parmfile_eastsplam
<edit the parmfile_eastsplam>
migrate-n parmfile_eastsplam -nomenu
```

the parmfile needs to have a different *custom-migration* setting and a change of the *population-relabel* option. Change it so that we have Africa → Asia → Americas the custom migration matrix should be a 3x3 matrix; in addition you will need to change the *population-relabel* option to pool Brazil and Mexico and Puerto Rico.

Once you edited your copy compare with this.

Model 7 to the west, to the east and splam

```
cp parmfile.template parmfile_twoways
perl -p -i -e 's/template/twoways/g;' parmfile_twoways
<edit the parmfile_twoways>
migrate-n parmfile_twoways -nomenu
```

the parmfile needs to have a different *custom-migration* setting and a change of the *population-relabel* option. Change it so that we have Africa → Asia → Americas **and** Africa → Americas the custom migration matrix should be a 3x3 matrix; in addition you will need to change the *population-relabel* option to pool Brazil and Mexico and Puerto Rico.

Once you edited your copy compare with this.

Model 8 pick your own model if you have time

```
cp parmfile.template parmfile_own
perl -p -i -e 's/template/own/g;' parmfile_own
<edit the parmfile_own>
migrate-n parmfile_own -nomenu
```

Design your own model!

Reporting

You have run several models and since we ran them not really long enough we want to see whether an average estimate of all students may give some intuition what is going on with the Zika virus. Each of the outfiles has a table of the marginal likelihoods. Report the value for your output files (you can report these before you have run all of them)

Report the number circled in **RED**. We will run an excel sheet to look at the model probabilities and marginal likelihoods reported by the class. [*last 30 minutes*]

Zika virus -- /

<i>Log-Probability of the data given the model (marginal likelihood)</i>			
Use this value for Bayes factor calculations: BF = Exp[ln(Prob(D thisModel) - ln(Prob(D otherModel)) or as LBF = 2 (ln(Prob(D thisModel) - ln(Prob(D otherModel)) shows the support for thisModel]			
Locus	TI(1a)	BTI(1b)	HS(3)
1	-31813.07	-26644.20	-27521.75
(1a) TI: Thermodynamic integration: log(Prob(D Model)): Good approximation with many temperatures (1b) BTI: Bezier-approximated Thermodynamic integration: when using few temperatures USE THIS! (2) SS: Steppingstone Sampling (Xie et al 2011) (3) HS: Harmonic mean approximation: Overestimates the marginal likelihood, poor variance			
Citation suggestions: Beerli P. and M. Palczewski, 2010. Unified framework to evaluate panmixia and migration direction among multiple sampling locations, <i>Genetics</i> , 185: 313-326. Palczewski M. and P. Beerli, 2014. Population model comparison using multi-locus datasets. In M.-H. Chen, L. Kuo, and P. O. Lewis, editors, <i>Bayesian Phylogenetics: Methods, Algorithms, and Applications</i> , pages 187-200. CRC Press, 2014. Xie W., P. O. Lewis, Y. Fan, L. Kuo, and M.-H. Chen. 2011. Improving marginal likelihood estimation for Bayesian phylogenetic model selection. <i>Systematic Biology</i> , 60(2):150–160, 2011.			

I have added a script that allows you to generate a table of the marginal likelihoods, the Bayes factors compared to the best model, and the model probabilities (probability weight). The script uses *grep* and a small *python* script that is doing the calculations. It will generate a table by extracting the marginal likelihoods from all **outfiles** in the directory. Call the script like this

```
./modelprohtable
```

Spoiler ALERT, if you click me before you have done the tutorial, you will see the order of the models and thus lose all the excitement about which model wins.