phyloflows: Estimating transmission flows under heterogeneous sampling - a first example

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This vignette gives a basic first introduction to estimating transmission flows with the `phyloflows` package.

Input data

phyloflows expects input data in a specific format.

- `dobs` a data.frame of observed transmission counts within and between population groups.
- `dprior` a data.frame that summarises prior information on how population groups were sampled.

To get you started, **phyloflows** comes with a small simulated example data set of transmission counts and sampling information between two population groups, denoted by “1” and “2”:

```
#   required R packages
require(phyloflows)
require(ggplot2)
require(bayesplot)
require(data.table)
require(coda)

#
#   load transmission flow data "twoGroupFlows1"
data(twoGroupFlows1, package="phyloflows")
#   observed transmission counts
dobs <- twoGroupFlows1$dobs
#   sampling information
dprior <- twoGroupFlows1$dprior
```

Input data: observed transmission flows

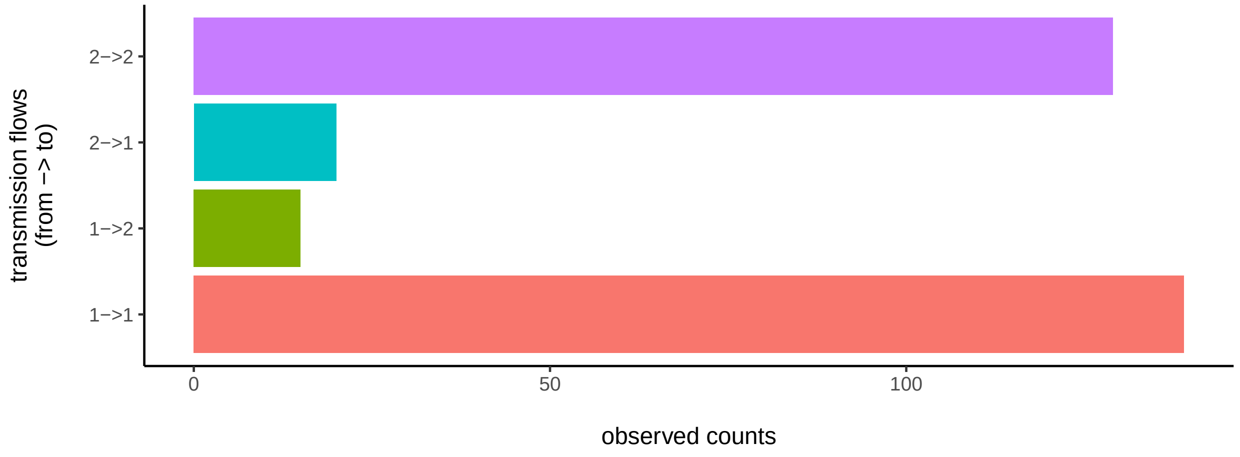
```
dobs
#>    REC_TRM_CATEGORY TR_TRM_CATEGORY TR_SAMPLING_CATEGORY REC_SAMPLING_CATEGORY TRM_OBS TRM_CAT_PAIR_
#> 1:                1               1                    1                     1     139
#> 2:                2               1                    1                     2      15
#> 3:                1               2                    2                     1      20
#> 4:                2               2                    2                     2     129
```

`dobs` specifies observed counts of transmissions from a transmitter group to a recipient group. It must contain the following columns:

- *TR_TRM_CATEGORY* name of transmitter group.
- *REC_TRM_CATEGORY* name of recipient group.
- *TRM_CAT_PAIR_ID* identifier of transmitter-recipient pair

- *TRM_OBS* observed transmission counts

Let us look at the data. The first row contains counts of transmission flows from group “1” to group “1”, and there are 139 of them. The next row contains counts of transmission flows from group “1” to group “2”, and there are 15 of them. Here is a barplot of our input data:



Input data: sampling information

`dobs` also must contain information about how each group was sampled. This is stored in the following columns:

- *TR_SAMPLING_CATEGORY* sampling strata of transmitter group
- *REC_SAMPLING_CATEGORY* sampling strata of recipient group

Each transmitter/recipient group is associated to a sampling category. This can be “sampling group a” for both “1” and “2”, or “a” and “b” respectively for “1” and “2”. In our little data set, we gave the same name to transmitter/recipient and sampling groups.

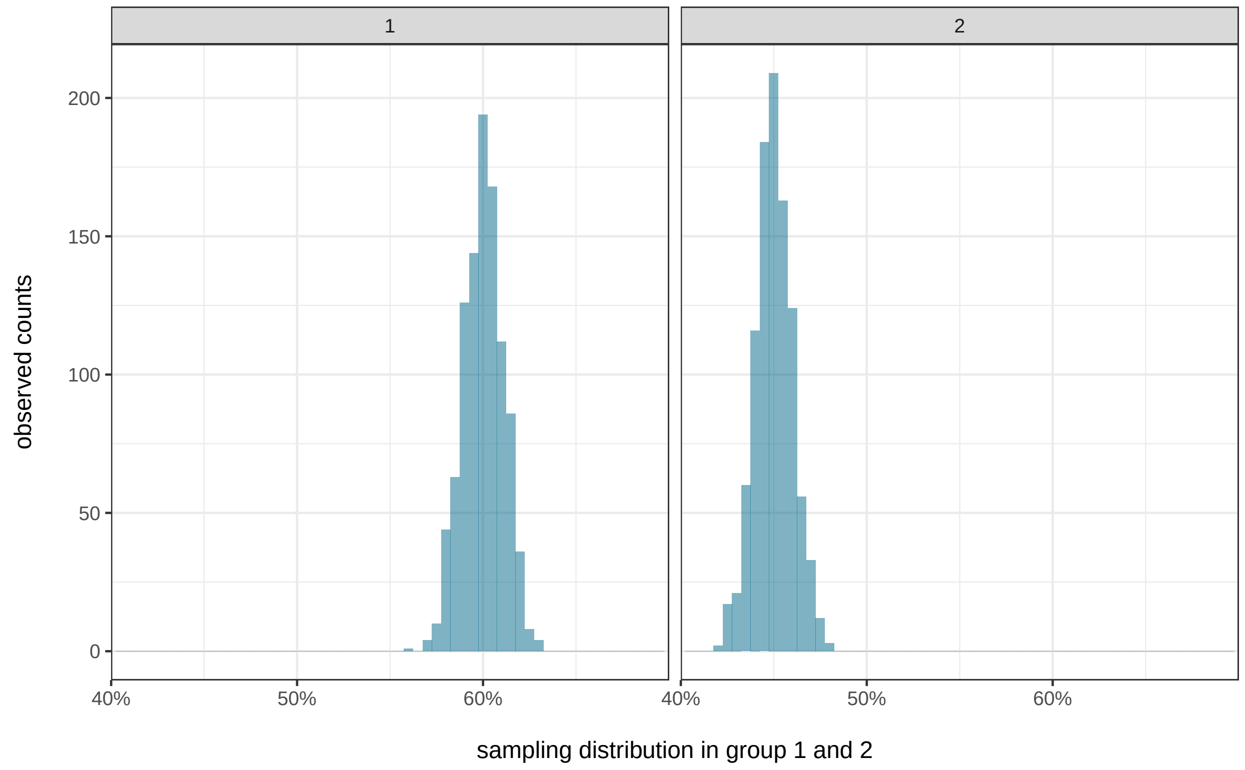
`dprior` specifies the probability of sampling an individual from each sampling group. To keep this as flexible as possible, samples from the sampling distribution, rather than say the mean and standard deviation, need to be given. This information is stored in the following columns:

- *SAMPLING_CATEGORY* name of sampling strata
- *SAMPLE* identifier of sample from the sampling distribution
- *P* sampling probability
- *LP* log density of the sampling probability under the sampling distribution.

Let us look at the sampling information:

```
head(dprior)
#>    SAMPLING_CATEGORY         P SAMPLE       LP
#> 1:                 1 0.5824160      1 2.318750
#> 2:                 1 0.6184042      2 2.168504
#> 3:                 1 0.6033518      3 3.548540
#> 4:                 1 0.6015475      4 3.585452
#> 5:                 1 0.5918721      5 3.321375
#> 6:                 1 0.6034198      6 3.546614
```

Here is a histogram of the sampling distribution from sampling groups “1” and “2”. Notice that in our example, the probability of sampling individuals in group “1” is higher than that among individuals in group “2”.



To capture different sampling probabilities for sources and recipients, the variable *WHO* can be used.

```
tmp= copy(dprior)
tmp[,WHO:='REC_SAMPLING_CATEGORY']
dprior[,WHO:='TR_SAMPLING_CATEGORY']
dprior <- rbind(dprior,tmp)
head(dprior)
#>    SAMPLING_CATEGORY         P SAMPLE       LP                  WHO
#> 1:                 1 0.5824160      1 2.318750 TR_SAMPLING_CATEGORY
#> 2:                 1 0.6184042      2 2.168504 TR_SAMPLING_CATEGORY
#> 3:                 1 0.6033518      3 3.548540 TR_SAMPLING_CATEGORY
#> 4:                 1 0.6015475      4 3.585452 TR_SAMPLING_CATEGORY
#> 5:                 1 0.5918721      5 3.321375 TR_SAMPLING_CATEGORY
#> 6:                 1 0.6034198      6 3.546614 TR_SAMPLING_CATEGORY
```

Statistical model

`phyloflows` uses a Bayesian approach to estimate the proportion of transmissions between the two population groups,

$$\pi = (\pi_{11}, \pi_{12}, \pi_{21}, \pi_{22}).$$

The model can be motivated as follows. Suppose the actual, unobserved number of transmissions from group i to group j are z_{ij}. Denote the vector of actual transmission counts by

$$z = (z_{11}, z_{12}, z_{21}, z_{22}).$$

We assume that transmission events occurred independently of each other. Then the likelihood of the actual transmission counts can be modelled by

$$p(z|Z, \pi) = Multinomial(z; Z, \pi),$$

where Z is the total number of transmissions, $Z = \sum_{kl} z_{kl}$. Next, we specify a model for observing one actual transmission event. We assume that sampling occurred at random within each of the sampling groups i and j. We then obtain

$$p(n_{ij}|z_{ij}, s_i, s_j) = Binomial(n_{ij}; z_{ij}, s_i * s_j),$$

where s_i is the probability of sampling an individual from group i, and similary for s_i.

These equations suggest that one approach to infer the proportion of transmissions π could be via data augmentation. In data augmentation, we would consider the unobserved, actual transmission counts z as latent variables, and then infer the joint posterior distribution of the parameters (z, Z, π) with a Monte Carlo algorithm.

However there is a more efficient approach for the particular model above. Inference of π under the Multinomial likelihood $Multinomial(z; Z, \pi)$ is equivalent to inference of Poisson mean rates λ

$$\lambda = (\lambda_{11}, \lambda_{12}, \lambda_{21}, \lambda_{22})$$

in the system of independent Poisson likelihoods

$$p(z_{ij}|\lambda_{ij}) = Poisson(z; \lambda_{ij}),$$

where $\lambda_{ij} > 0$, $i = 1, 2$ and $j = 1, 2$. The proportion of transmissions π are recovered via the equations

$$\pi_{ij} = \lambda_{ij} / \sum_{k=1,2;l=1,2} \lambda_{kl}.$$

for $i = 1, 2$ and $j = 1, 2$. This is known as the Poisson trick. The advantage of this model parameterisation is that sampled Poisson random variables are again Poisson random variables, which allows us to integrate out analytically the unknown, actual transmission counts z_{ij}. We obtain

$$p(n|\lambda, s) = \prod_{i=1,2;j=1,2} Poisson(n_{ij}; \lambda_{ij} * s_i * s_j).$$

The free parameters of the model are (λ, s), and the posterior distribution of the free parameters is given by

$$\begin{aligned} p(\lambda, s|n) &\propto p(n|\lambda, s)p(\lambda, s) \\ &= \prod_{i=1,2;j=1,2} Poisson(n_{ij}; \lambda_{ij} * s_i * s_j)p(\lambda_{ij})p(s_i)p(s_j). \end{aligned}$$

For the prior distributions, we specify for $p(\lambda_{ij})$, $i = 1, 2; j = 1, 2$ uninformative prior distributions. We use a Gamma distribution with parameters $\alpha_i = 0.8/4$ and $\beta = 0.8/Z$ with $Z = \sum_{ij|n_{ij}>0} n_{ij}/(s_i * s_j) + \sum_{ij|n_{ij}>0}(1 - s_i * s_j)/(s_i * s_j)$. This choice implies for π a Dirichlet prior distribution with parameters α_i, which is considered to be an objective choice. For $p(s_i)$, we use a strongly informative prior distribution, based on the available data as illustrated above.

MCMC

MCMC syntax

We use a Markov Chain Monte Carlo algorithm to sample from the posterior distribution

$$p(\lambda, s|n) \propto \prod_{i=1,2;j=1,2} Poisson(n_{ij}; \lambda_{ij} * s_i * s_j)p(\lambda_{ij})p(s_i)p(s_j).$$

Then, we calculate the main quantity of interest, π, via

$$\pi_{ij} = \lambda_{ij} / \sum_{k=1,2;l=1,2} \lambda_{kl}.$$

for $i = 1, 2$ and $j = 1, 2$. The syntax for running the algorithm is as follows.

```
# specify a list of control variables:
#   seed    random number seed
#   mcmc.n  number of MCMC iterations
#   verbose flag for verbose output
#   outfile output file name if you like to have the results
#           written to an *.rda* file
control <- list(seed=42, mcmc.n=500, verbose=0)
# run MCMC
ans <- source.attribution.mcmc(dobs, dprior, control)
#>
#> Setting seed to 42
#> Number of parameters:     8
#> Dimension of PI:  4
#> Sweep length:     4
#> Number of sweeps:     125
#> Number of iterations:     500
#> Sweeps done:  100
#> Sweeps done:  125
```

MCMC messages

Let s have a look at the output messages.

- `Setting seed to 42`: This tells us the random number seed that was used, so we can re-run the algorithm to get identical results.
- `Number of parameters: 6`: The total number of unknown parameters in the MCMC is the length of λ plus length of the sampling probabilities s. Here, the number of flows between the two subpopulation is 4, and sampling was different in each subpopulation, adding 2 parameters.
- `Dimension of PI: 4`: the number of flows between the two subpopulations is 4.
- `Sweep length: 4`: the MCMC updates in turn a subset of the sampling probabilities of transmission groups

$$\xi = (\xi_{11}, \xi_{12}, \xi_{21}, \xi_{22}), \qquad \xi_{ij} = s_i * s_j,$$

  which is followed by an update of the entire vector of Poisson transmission rates λ. The subset of ξ that is updated is specified as follows. For each population group i, we determine all components of ξ that involve s_i. In our example, for $i = 1$, the components of ξ to update are $(\xi_{11}, \xi_{12}, \xi_{21})$; and for $i = 2$, the components of ξ to update are $(\xi_{12}, \xi_{21}, \xi_{22})$. An MCMC sweep counts the number of MCMC iterations needed in order to update all parameters at least once. In our case, we have 2 updates on components of ξ, and after each we update λ, so the sweep length is 4.
- `Number of sweeps: 125`: The total number of sweeps is determined from `control[['mcmc.n']]`, by dividing `control[['mcmc.n']]` with the sweep length, and possibly rounding up.
- `Number of iterations: 500`: The total number of iterations is set to the number of sweeps (given above), multiplied by the sweep length. This may differ slightly from `control[['mcmc.n']]` because we round up the number of sweeps to the next integer.

MCMC output

Let us have a look at the output:

```
str(ans)
#> List of 13
#>  $ with.sampling: logi TRUE
#>  $ time         : 'difftime' num 9.80948901176453
#>   ..- attr(*, "units")= chr "secs"
#>  $ dlu           :Classes 'data.table' and 'data.frame':  4 obs. of  3 variables:
#>   ..$ WHO              : Factor w/ 2 levels "TR_SAMPLING_CATEGORY",..: 1 1 2 2
#>   ..$ SAMPLING_CATEGORY: num [1:4] 1 2 1 2
#>   ..$ UPDATE_ID        : int [1:4] 1 2 3 4
#>   ..- attr(*, ".internal.selfref")=<externalptr>
#>   ..- attr(*, "sorted")= chr "UPDATE_ID"
#>  $ dlt           :Classes 'data.table' and 'data.frame':  4 obs. of  4 variables:
#>   ..$ TRM_CAT_PAIR_ID: int [1:4] 1 2 3 4
#>   ..$ TRM_OBS        : int [1:4] 139 15 20 129
#>   ..$ TR_UPDATE_ID   : int [1:4] 1 1 2 2
#>   ..$ REC_UPDATE_ID  : int [1:4] 3 4 3 4
#>   ..- attr(*, ".internal.selfref")=<externalptr>
#>   ..- attr(*, "sorted")= chr "TRM_CAT_PAIR_ID"
#>   ..- attr(*, "index")= int(0)
#>   .. ..- attr(*, "__TR_UPDATE_ID")= int(0)
#>   .. ..- attr(*, "__REC_UPDATE_ID")= int [1:4] 1 3 2 4
#>  $ nprior       : int 1000
#>  $ sweep        : int 4
#>  $ nsweep       : num 125
#>  $ n            : num 500
#>  $ sweep_group  : num 125
#>  $ pars         :List of 7
#>   ..$ ALPHA     : num [1, 1:4] 0.2 0.2 0.2 0.2
#>   ..$ BETA      : num [1:126, 1] 0.000746 0.000689 0.000682 0.000714 0.000683 ...
#>   ..$ XI        : num [1:126, 1:4] 0.612 0.585 0.597 0.604 0.583 ...
#>   ..$ XI_LP     : num [1:126, 1:4] 3.04 2.62 3.57 3.54 2.46 ...
#>   ..$ S         : num [1:126, 1:4] 0.374 0.353 0.362 0.362 0.35 ...
#>   ..$ S_LP      : num [1:126, 1:4] 6.07 6.16 7.03 7.13 6.06 ...
#>   ..$ LOG_LAMBDA: num [1:126, 1:4] 6.04 5.95 5.93 5.86 6 ...
#>  $ it.info      :Classes 'data.table' and 'data.frame':  501 obs. of  7 variables:
#>   ..$ IT       : int [1:501] 0 1 2 3 4 5 6 7 8 9 ...
#>   ..$ PAR_ID   : int [1:501] 0 1 2 3 4 1 2 3 4 1 ...
#>   ..$ BLOCK    : chr [1:501] "INIT" "XI-LAMBDA" "XI-LAMBDA" "XI-LAMBDA" ...
#>   ..$ MHRATIO  : num [1:501] 1 1 0.999 1 0.998 ...
#>   ..$ ACCEPT   : int [1:501] 1 1 1 1 1 1 1 1 1 1 ...
#>   ..$ LOG_LKL  : num [1:501] -13.6 -12.6 -12.5 -12.8 -12.4 ...
#>   ..$ LOG_PRIOR: num [1:501] -20.6 -20.7 -18.3 -18 -16.1 ...
#>   ..- attr(*, ".internal.selfref")=<externalptr>
#>  $ curr.it      : int 501
#>  $ curr.it.adj  : int 501
```

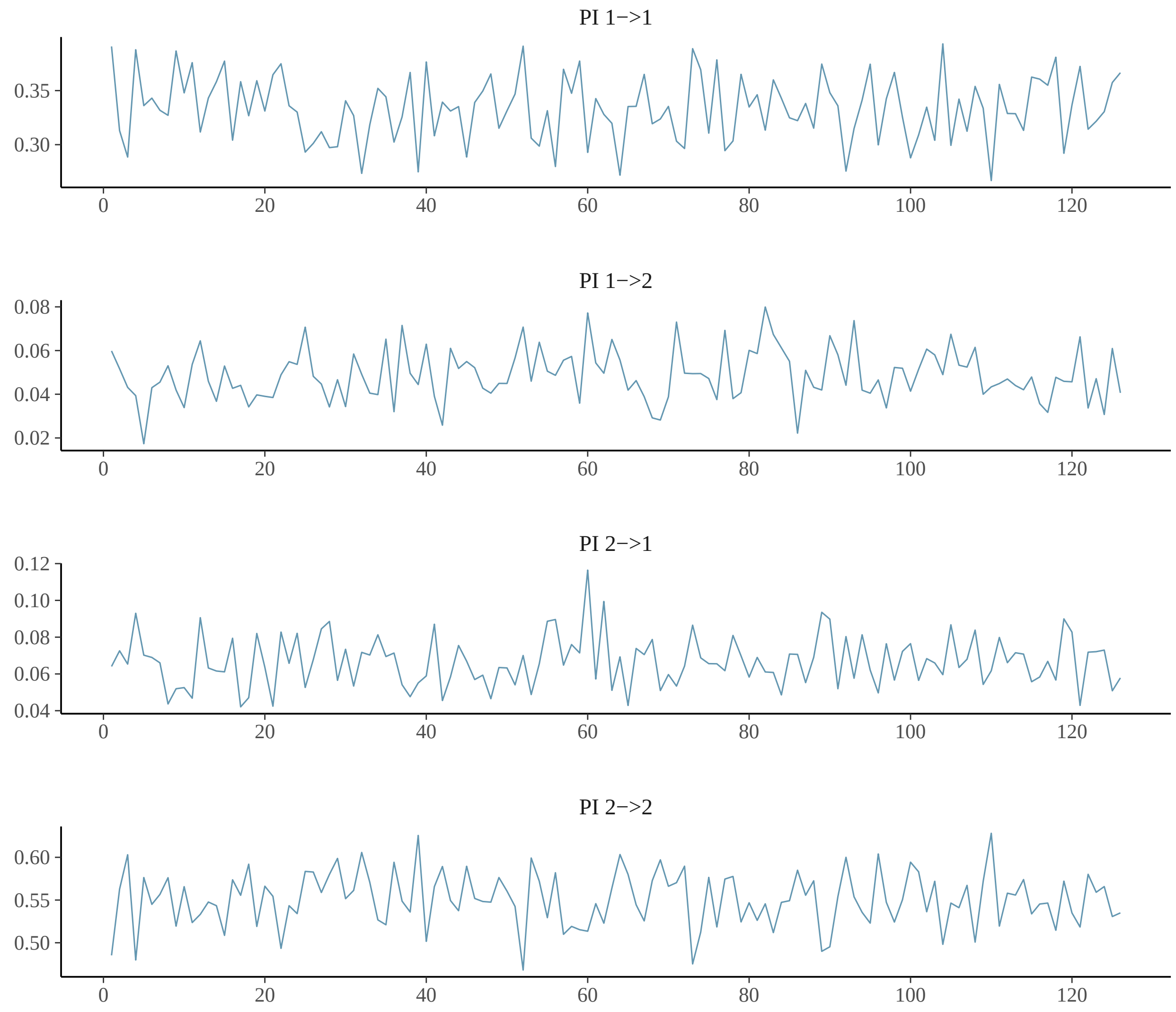
We are mostly interested in the marginal posterior distribution

$$p(\pi|n),$$

and the algorithm returns samples of $\log \lambda$. Let us calculate the transmission flows π from the log Poisson rates, and make a trace plot:

```
#   transform lambda to pi
tmp <- exp(ans[['pars']][['LOG_LAMBDA']])
posterior.pi <- t(apply(tmp, 1, function(rw) rw/sum(rw)))
#   make column names
setkey(dobs, TRM_CAT_PAIR_ID) #order by pair IDs
post.pi.colnames <- paste0('PI ',dobs$TR_TRM_CATEGORY,'->',dobs$REC_TRM_CATEGORY)
colnames(posterior.pi) <- post.pi.colnames
```

```
#   plot mcmc trajectories
bayesplot:::mcmc_trace( posterior.pi,
                        pars=colnames(posterior.pi),
                        facet_args = list(ncol = 1),
                        n_warmup=0)
```



Notice that the posterior estimate for transmissions within group "2" is about 55%. This is considerably larger than the raw estimate from the observed transmission counts, 129/303=43%, because individuals in group "2" have lower probability of being sampled than those in group "1".

That's it for now. Of course we would like to run the MCMC chain for longer, perhaps 10,000 sweeps. We would also like to check for convergence, calculate effective sample sizes, and quantiles of the posterior distribution. But this is for later. Use your R wizardry to process the output further, and have a look at the other vignettes.