

Metabarcoding model development in NIMBLE

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The model

We know the total number of reads N_{reads} , the number of species S , the total number of individuals N , and the correlation structure from the phylogeny Σ_{phy} . We also know the vector of number of reads per species x_{read} . We do not know the rate of copy number evolution σ_{copy} nor the rate of primer affinity evolution σ_{primer} . We also most importantly don't know the actual vector of abundances x . We want to model the number of reads as multinomial conditioned on N_{reads} and S , and with a probability vector p given by

$$p \sim \text{dir}(x\nu\lambda)$$

where ν is a variable proportional to copy number and λ is a variable proportional to primer affinity. We will assume that $\log\nu$ evolved according to a Brownian motion process with rate σ_{copy} and mean $\mu_{copy} = 0$. We will assume that $\text{logit}_{\min=\rho}(\lambda)$ evolved according to an independent Brownian motion process with rate σ_{primer} and mean $\mu_{primer} = 0$. $\text{logit}_{\min=\rho}$ is a modified *logit* function which assumes λ is constrained by a lower bound $0 \leq \rho \leq 1$. Its corresponding modified *expit* function is

$$\text{expit}_{\min=\rho}(x) = \rho + \frac{1 - \rho}{1 + \exp(-x)}$$

The variance-covariance matrix for a Brownian-motion process on a known phylogeny is given as

$$\Sigma_{i,j} = \sigma D_{MRCA(i,j)}$$

where $D_{MRCA(i,j)}$ is the distance from the root to the most recent common ancestor of tips i and j . $D_{MRCA(i,i)}$ is simply the depth of the root.

Thus our full model is

$$x_{reads} \sim \text{multinom}(N_{reads}, p_1, \dots, p_S)$$

where

$$p \sim \text{dir}(x\nu\lambda)$$

and ν and λ are distributed

$$\log(\nu) \sim \text{mvnorm}(0, \sigma_{copy} d_{MRCA(i,j)})$$

$$\text{logit}_{\min=\rho}(\lambda) \sim \text{mvnorm}(0, \sigma_{primer} d_{MRCA(i,j)})$$

The priors for this hierarchical model are

$$x/N \sim \text{dir}(N/S, \dots, N/S)$$

$$\frac{1}{\sigma_{copy}^2} \sim \Gamma(0.001, 0.001)$$

$$\frac{1}{\sigma_{primer}^2} \sim \Gamma(0.001, 0.001)$$

$$\rho \sim \text{unif}(0, 1)$$

NIMBLE model

We first simulate some data that will be needed in the model specification:

- **S** number of species to simulate
- **tre** is the underlying phylogeny
- **N** is the number of actual individuals
- **Nreads** is the total number of reads
- **numberReads** is a vector of the number of reads assigned to each spp

```
# simulation functions
source('~/.Dropbox/hawaiiDimensions/mol2ecol/simMetaBar.R')

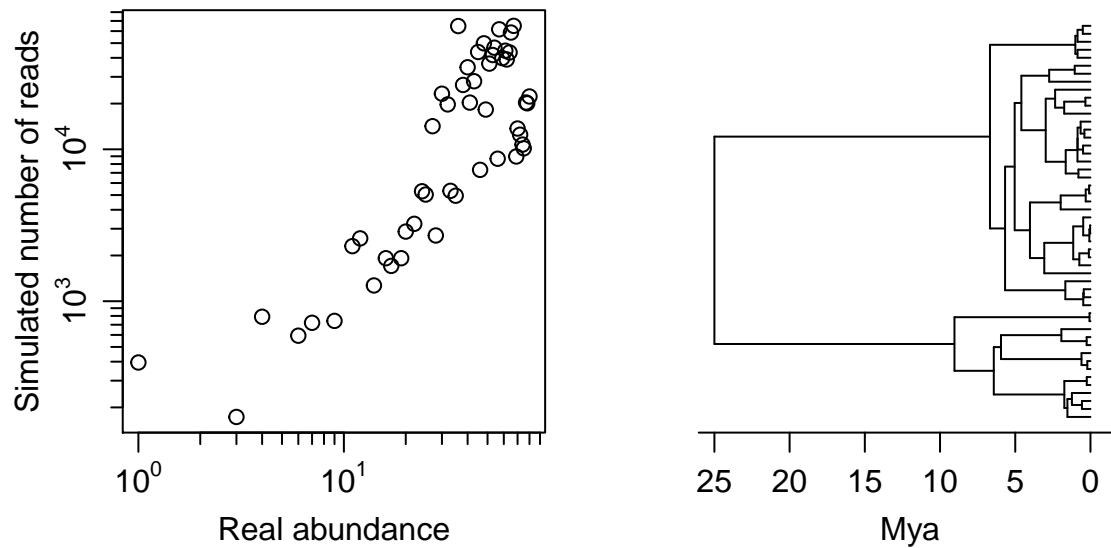
# set parameters for simulation
S <- 50
n <- round(seq(1, 80, length.out = S))
N <- sum(n)
Nreads <- 1e+06
sigCopy <- 0.1
sigPrimer <- 0.05
minAffin <- 0.8

# simulate phylogeny and number of reads resulting from metabarcoding
set.seed(1)
sim <- simMetaBar(abund = n, minAffin = minAffin,
                  sigCopy = sigCopy, sigPrimer = sigPrimer,
                  nreads = Nreads)

# extract needed objects from output
numberReads <- sim$reads
tre <- sim$tre
```

Let's quickly check the simulation to see that it's reasonable

```
library(socorro)
par(mfrow = c(1, 2), mar = c(3, 3, 0, 0) + 0.5, mgp = c(2, 0.75, 0))
plot(sim$abund, numberReads, xlab = 'Real abundance', ylab = 'Simulated number of reads',
     log = 'xy', axes = FALSE, frame.plot = TRUE)
logAxis(1, expLab = TRUE); logAxis(2, expLab = TRUE)
plot(tre, show.tip.label = FALSE)
axis(1, at = pretty(par('usr')[1:2]), labels = rev(pretty(par('usr')[1:2])))
mtext('Mya', side = 1, line = 2)
```



To specify our model in NIMBLE we can define and use custom multinomial-Dirichlet functions:

```
library(nimble)

ddirchmulti <- nimbleFunction(
  run = function(x = double(1), alpha = double(1), size = double(0),
    log = integer(0, default = 0)) {
    returnType(double(0))
    alpha0 <- sum(alpha)

    # new log prob that ignores 0's instead of throwing NaN/Inf
    lgammaSum <- numeric(length = length(x), value = 0, init = TRUE)
    for(i in 1:length(lgammaSum)) {
      if(x[i] > 0) {
        lgammaSum[i] <- log(x[i]) + lgamma(alpha[i]) +
          lgamma(x[i]) -
          lgamma(alpha[i] + x[i])
      }
    }
    logProb <- log(size) +
      lgamma(alpha0) + lgamma(size) - lgamma(alpha0 + size) -
      sum(lgammaSum)

    if(log) return(logProb)
    else return(exp(logProb))
  }
)

rdirchmulti <- nimbleFunction(
  run = function(n = double(0, default = 1), alpha = double(1), size = double(0)) {
    returnType(double(1))

    # modified from MCMCpack to allow alpha_k = 0
    x <- numeric(length = length(alpha), value = 0, init = TRUE)
    for(i in 1:length(x)) x[i] <- rgamma(1, shape = alpha[i], rate = 1)
    p <- x/sum(x)
  }
)
```

```

    return(rmulti(1, size = size, prob = p))
  }
)

```

The arguments are:

- **x** vector of values (e.g. number of reads for each species x_{reads})
- **alpha** vector of parameters of the Dirichlet distribution
- **size** number of trials (e.g. total number of reads N_{reads})
- **n** number of observations (only $n = 1$ supported)

We can now specify the model:

```

mod <- nimbleCode({
  # p is proportion of total abundance for each spp
  x[1:S] <- N*p[1:S]

  # define phylogenetically-correlated copy number (nu) and primer affinity (lambda)
  # Note: tauCopy and tauPrimer are inverse variances, and 'Prec' stands for
  # 'Precession' matrix (the inverse of the var-covar matrix)
  # Note: var-cov matrix D is defined in constants, as is mu0 (which is a vector of 0)
  PrecCopy[1:S, 1:S] <- tauCopy * Dinv[1:S, 1:S]
  PrecPrimer[1:S, 1:S] <- tauPrimer * Dinv[1:S, 1:S]
  logNu[1:S] ~ dmnorm(mu0[1:S], PrecCopy[1:S, 1:S])
  logitLambda[1:S] ~ dmnorm(mu0[1:S], PrecPrimer[1:S, 1:S])
  nu[1:S] <- exp(logNu[1:S])
  lambda[1:S] <- rho + (1 - rho) / (1 + exp(-logitLambda[1:S]))

  # define dirichlet-multinom params and the distribution of x_{reads}
  alpha[1:S] <- x[1:S] * nu[1:S] * lambda[1:S]
  xreads[1:S] ~ ddirchmulti(alpha[1:S], Nreads)

  # priors
  p[1:S] ~ ddirch(p0[1:S]) # p0 defined in constants
  tauCopy ~ dgamma(0.001, 0.001)
  tauPrimer ~ dgamma(0.001, 0.001)
  rho ~ dunif(0, 1)
})

```

And initialize the model

```

# model constants, data and inits
S <- length(tre$tip.label)
modConstants <- list(S = S, N = N, Nreads = Nreads,
                    Dinv = solve(vcv(tre)), # vcv gives the vcov mat of a phylo for sig = 1
                    mu0 = rep(0, S), p0 = rep(N/S, S))
modData <- list(xreads = numberReads)
modInits <- list(
  # priors
  p = rep(1/modConstants$S, modConstants$S), tauCopy = 1, tauPrimer = 1, rho = 0.5,

  # deterministic relationships
  x = rep(modConstants$N/modConstants$S, modConstants$S),
  PrecCopy = modConstants$Dinv, PrecPrimer = modConstants$Dinv,

  # hyper distributions

```

```

logNu = rep(0, modConstants$S), logitLambda = rep(0, modConstants$S),

  # deterministic relationships arising from hyperdistributions
  nu = rep(1, modConstants$S), lambda = rep(0.75, modConstants$S)
)

# build model
mod <- nimbleModel(code = mod, name = 'mod', constants = modConstants,
                  data = modData, inits = modInits)

```

defining model...

Registering the following user-provided distributions: ddirchmulti .

NIMBLE has registered ddirchmulti as a distribution based on its use in BUGS code. Note that if you

Adding Dinv,mu0,p0 as data for building model.

building model...

setting data and initial values...

running calculate on model (any error reports that follow may simply

reflect missing values in model variables) ...

##

checking model sizes and dimensions...

##

model building finished.

Now we can compile and run the model

```

Cmod <- compileNimble(mod)
modConf <- configureMCMC(mod)
modConf$setThin(1)

```