

# Bayesian inference for a population growth model of the chytrid fungus

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## 1 Preliminaries

This examples assumes that **deBInfer** is installed and loaded. If this is not the case it needs to be installed from github, which requires the devtools package.

```
install.packages("devtools")
```

```
#Load the devtools package.  
library(devtools)
```

Then deBInfer can be installed from github.

```
install_github("pboesu/debinfer")
```

```
library(deBInfer)
```

## 2 The chytrid population growth model

Our example demonstrates parameter inference for a DDE model of population growth in the environmentally sensitive fungal pathogen *Batrachochytrium dendrobatidis* (Bd), which causes the amphibian disease chytridiomycosis (Rosenblum et al. 2010; Voyles et al. 2012). This model has been used to further our understanding of pathogen responses to changing environmental conditions. Further details about the model development, and the experimental procedures yielding the data used for parameter inference can be found in (Voyles et al. 2012).

The model follows the dynamics of the concentration of an initial cohort of zoospores,  $C$ , the concentration of zoospore-producing sporangia,  $S$ , and the concentration of zoospores in the next generation  $Z$ . The initial cohort of zoospores,  $C$ , starts at a known concentration, and zoospores in this initial cohort settle and become sporangia at rate  $s_r$ , or die at rate  $\mu_Z$ .  $f_s$  is the fraction of sporangia that survive to the zoospore-producing stage. We assume that it takes a minimum of  $T_{min}$  days before the sporangia produce zoospores, after which they produce zoospores at rate  $\eta$ . Zoospore-producing sporangia die at rate  $d_s$ . The concentration of zoospores,  $Z$ , is the only state variable measured in the experiments, and it is assumed that these zoospores settle ( $s_r$ ) or die ( $\mu_Z$ ) at the same rates as the initial cohort of zoospores.

### 2.1 DDE model

The equations that describe the population dynamics are as follows:

$$\frac{dC}{dt} = -(s_r + \mu_Z)C(t) \quad (1)$$

$$\frac{dS}{dt} = s_r f_s C(t - T_{min}) - d_s S(t) \quad (2)$$

$$\frac{dZ}{dt} = \eta S(t) - (s_r + \mu_Z)Z(t) \quad (3)$$

We can implement this system of differential equations for the `deSolve::dede` solver as follows. More details on how to specify differential equations for this solver can be found in the package documentation and vignettes (Soetaert, Petzoldt, and Setzer 2010).

```
#dede version
CSZ.dede<-function(t,y,p){

  sr    <-p["sr"]
  fs    <-p["fs"]
  ds    <-p["ds"]
  eta   <-p["eta"]
  Tmin  <-p["Tmin"]
  ##Tmax <-p["Tmax"]
  muz   <-p["muz"]

  Rs<-Ms<-0
  lag1<-lag2<-0

  if (t>Tmin){
    lag1<-lagvalue(t-Tmin)
    Rs <- sr*fs*lag1[1]
  }

  phiZ <- eta*y[2]
  dy1 <- -(muz+sr)*y[1]
  dy2 <- Rs - Ms - ds*y[2]
  dy3 <- phiZ - (muz+sr)*y[3]

  if(y[1]<0) dy1<-0
  if(y[2]<0){
    dy2 <- Rs - Ms
    dy3 <- -(muz+sr)*y[3]
  }
  if(y[3]<0){
    dy3 <- dy3+(muz+sr)*y[3]
  }

  list(c(dy1,dy2,dy3))
}
```

## 2.2 Observation model

Eventhough the data used in this example come from an experimental study, the system is only partially observed. We know the initial conditions for all states, but we only have observations for the second generation of Zoospores  $Z$ . Because the observations are counts (i.e. discrete numbers), we assume that observations of

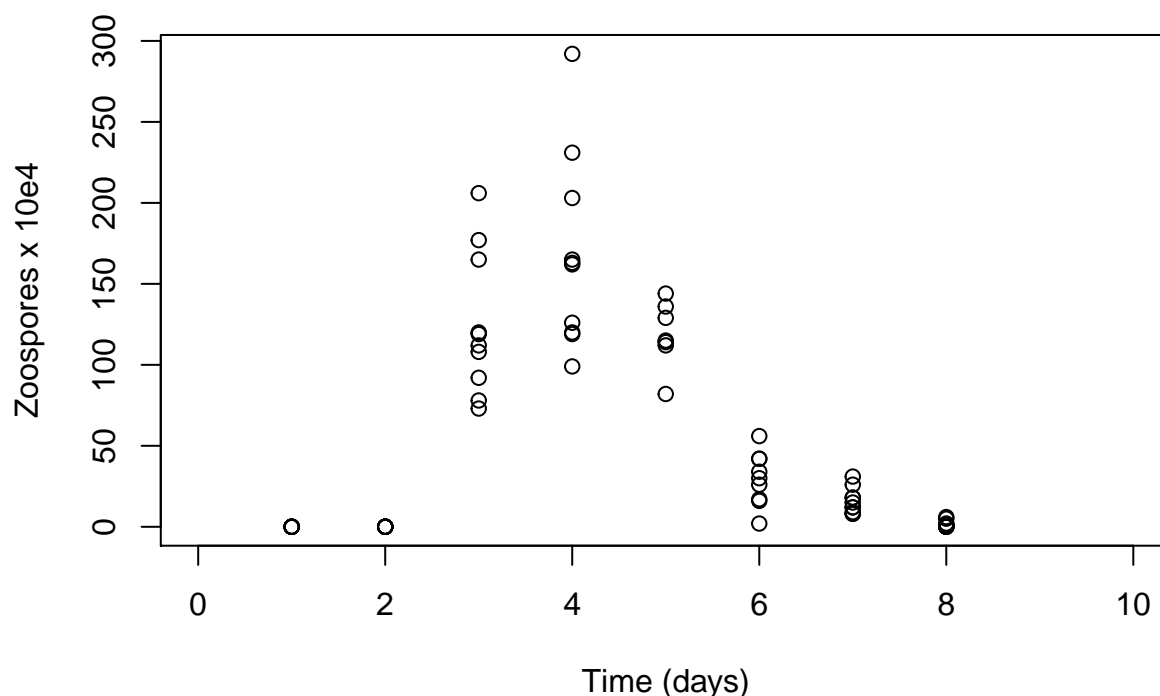
the system at a set of discrete times  $t'$  are independent Poisson random variables with a mean given by the solution of the DDE, at times  $t'$ .

The observations are provided with **deBInfer**. They can be loaded with the **data()** command.

```
#load chytrid data
data(chytrid)
#have a look at the variables
head(chytrid)
```

```
##      time count
## 1      1      0
## 2      1      0
## 3      1      0
## 4      1      0
## 5      1      0
## 6      1      0
```

```
#plot the data
plot(chytrid, xlab='Time (days)', ylab='Zoospores x 10e4', xlim=c(0,10))
```



The log-likelihood of the data given the parameters, underlying model, and initial conditions is then a sum over the  $n$  observations at each time point in  $t'$

$$\ell(\mathbf{Z}|\theta) = \sum_t^n Z_t \log \lambda - n\lambda \quad (4)$$

### Explain epsilon correction

This can be translated into an observation model function for **deBInfer**. The observation model function must have three named arguments **data**, **sim.data**, and **samp**, as these are used by the MCMC procedure

to pass in the data (as a `data.frame`), the current state of the Markov chain (as a named vector), and the associated DE model solution (as a matrix-like object of class `deSolve`). We can access these inputs to define the data likelihood. In this case we have repeat measurements for each time point, so we iterate over the unique timepoints in `data$time`, and then calculate the sum log-likelihood over all matching `data$count` observations using the current value of the state variable `Z` from the DE model solution at this point in the Markov chain.

```
# observation model
chytrid_obs_model<-function(data, sim.data, samp){

  ec<-0.01
  llik.Z<-0
  for(i in unique(data$time)){
    try(llik.Z<-llik.Z + sum(dpois(data$count[data$time==i],
                                  lambda=(sim.data[, 'Z'][sim.data[, 'time']==i]+ec),
                                  log=TRUE)))
  }
  llik<-llik.Z
  return(llik)
}
```

We continue by defining the parameters for inference

```
sr <- debinfer_par(name = "sr", var.type = "de", fixed = FALSE,
  value = 2, prior="gamma", hypers=list(shape = 5, rate = 1),
  prop.var=c(3,4), samp.type="rw-unif")

fs <- debinfer_par(name = "fs", var.type = "de", fixed = FALSE,
  value = 0.5, prior="beta", hypers=list(shape1 = 1, shape2 = 1),
  prop.var=0.01, samp.type="ind")

ds <- debinfer_par(name = "ds", var.type = "de", fixed = FALSE,
  value = 2, prior="gamma", hypers=list(shape = 1, rate = 1),
  prop.var=0.1, samp.type="rw")

muz <- debinfer_par(name = "muz", var.type = "de", fixed = FALSE,
  value = 1, prior="gamma", hypers=list(shape = 5, rate = 1),
  prop.var=c(4,5), samp.type="rw-unif")

eta <- debinfer_par(name = "eta", var.type = "de", fixed = FALSE,
  value = 10, prior="gamma", hypers=list(shape = 1, rate = 0.25),
  prop.var=5, samp.type="rw")

Tmin <- debinfer_par(name = "Tmin", var.type = "de", fixed = FALSE,
  value = 3, prior="unif", hypers=list(min = 2, max = 6),
  prop.var=0.05, samp.type="rw")

# ----inits-----
C <- debinfer_par(name = "C", var.type = "init", fixed = TRUE, value = 120)
S <- debinfer_par(name = "S", var.type = "init", fixed = TRUE, value = 0)
Z <- debinfer_par(name = "Z", var.type = "init", fixed = TRUE, value = 0)
```

Explain importance of init order

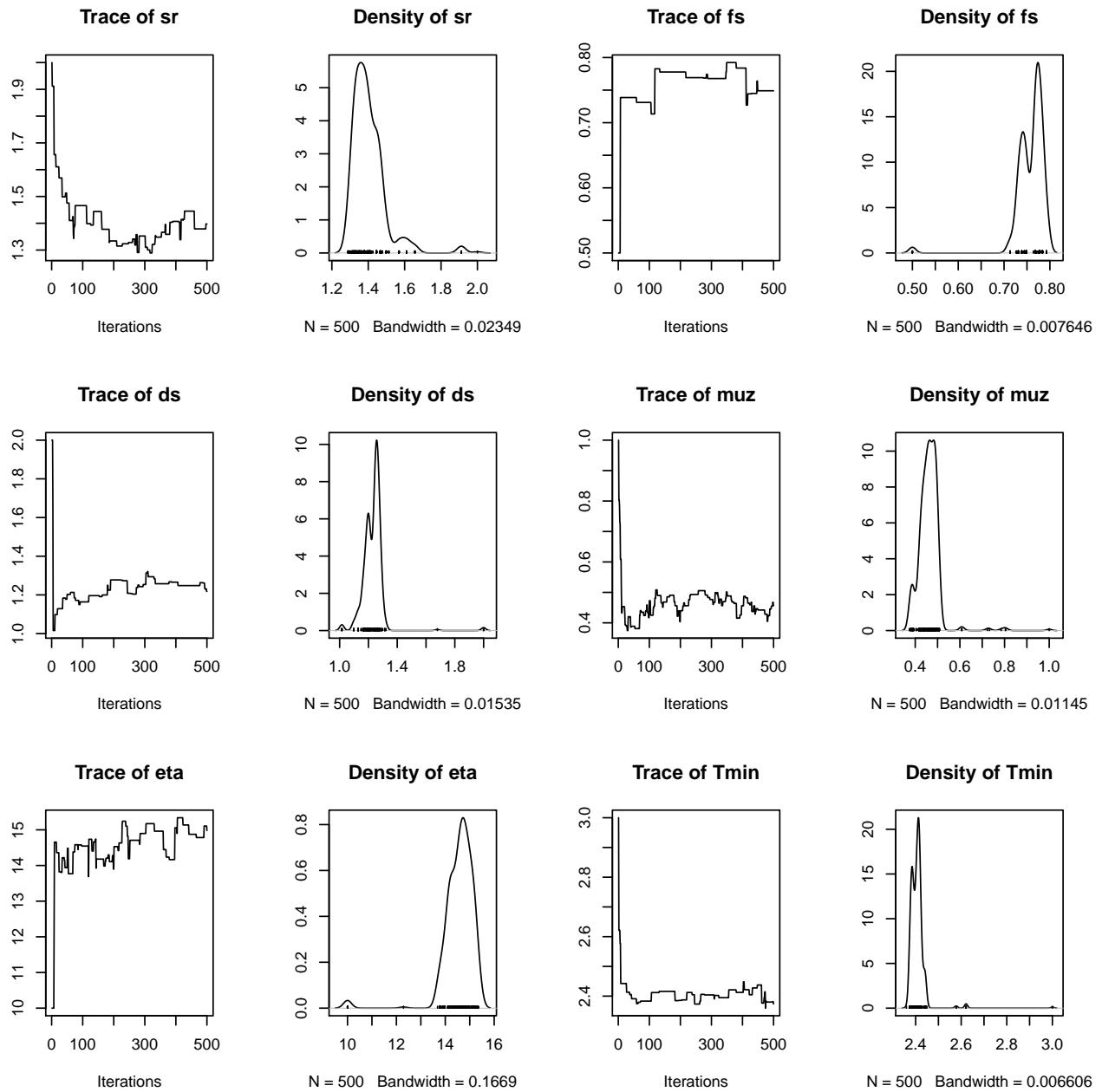
```
# ----setup-----
mcmc.pars <- setup_debinfer(sr, fs, ds, muz, eta, Tmin, C, S, Z)
```

And then do the actual inference

```
# do inference with deBInfer
# MCMC iterations
iter = 500
# inference call
dede_rev <- de_mcmc(N = iter, data=chytrid, de.model=CSZ.dede,
                    obs.model=chytrid_obs_model, all.params=mcmc.pars,
                    Tmax = max(chytrid$time), data.times=c(0,chytrid$time), cnt=iter %% 10,
                    plot=FALSE, sizestep=0.1, solver="dede", verbose = TRUE)
```

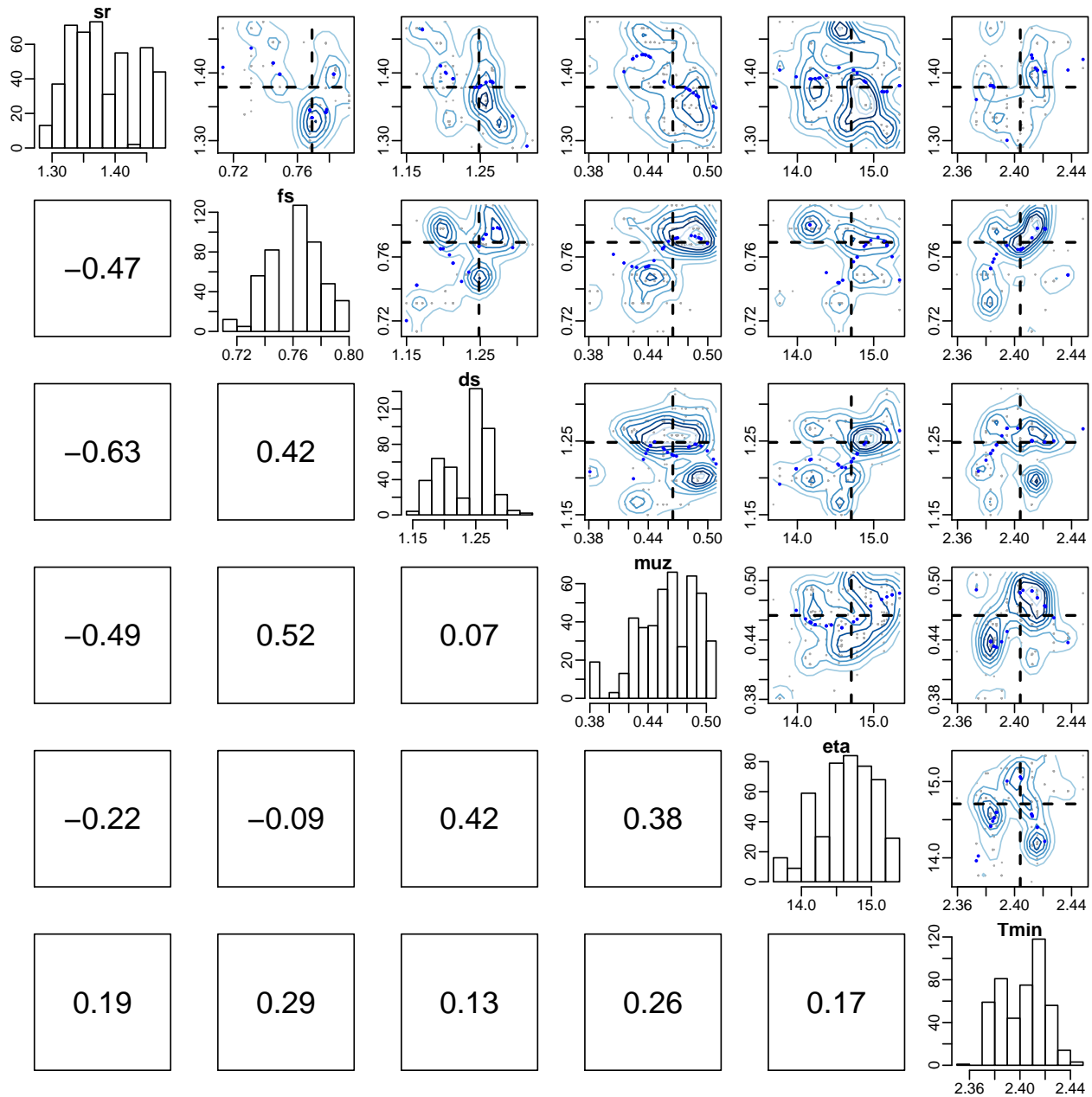
We plot and summarize the MCMC chains

```
par(mfrow = c(3,4))
plot(dede_rev, ask=FALSE, auto.layout=FALSE)
```

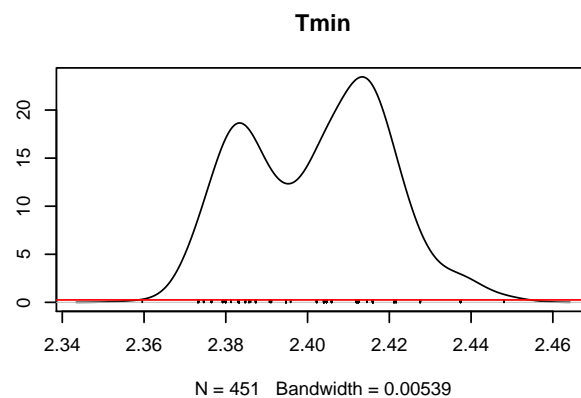
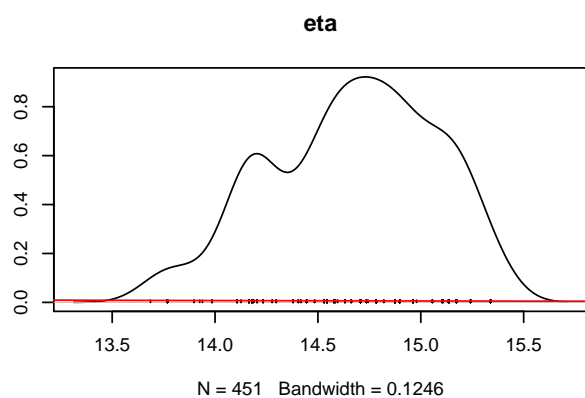
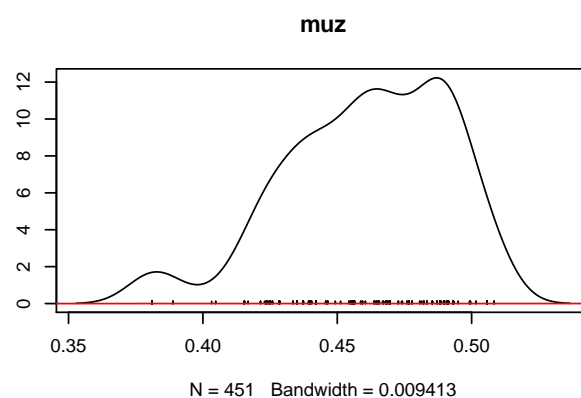
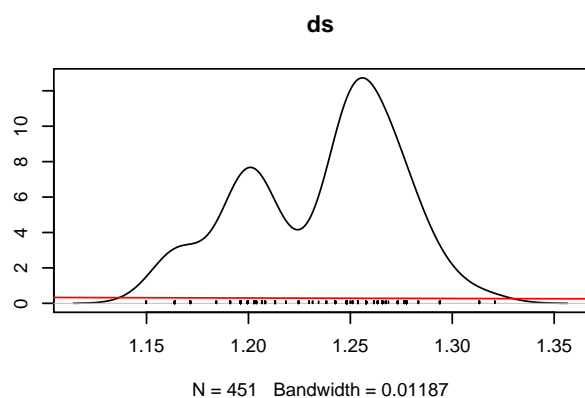
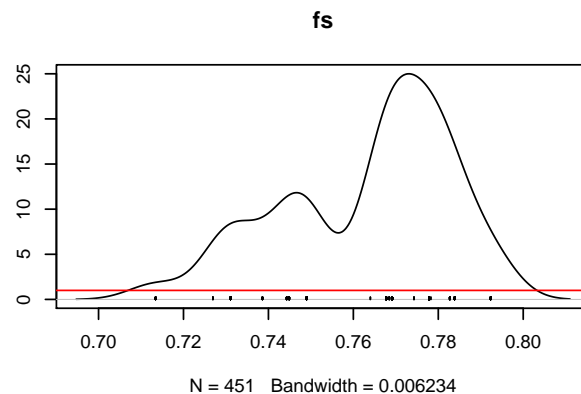
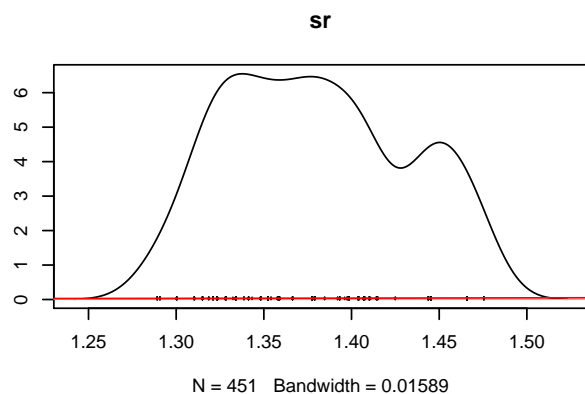


From the traceplot we can see that the burnin period is **about 200 samples**. We can remove the burnin and have a look at parameter correlations, and the overlap between the posterior and prior densities.

```
burnin = 50
pairs(dede_rev, burnin = burnin, scatter=TRUE, trend=TRUE)
```



```
post_prior_densplot(dede_rev, burnin = burnin)
```



```
summary(dede_rev)
```

```
##
## Iterations = 1:500
## Thinning interval = 1
## Number of chains = 1
## Sample size per chain = 500
##
## 1. Empirical mean and standard deviation for each variable,
##    plus standard error of the mean:
##
##      Mean      SD Naive SE Time-series SE
```



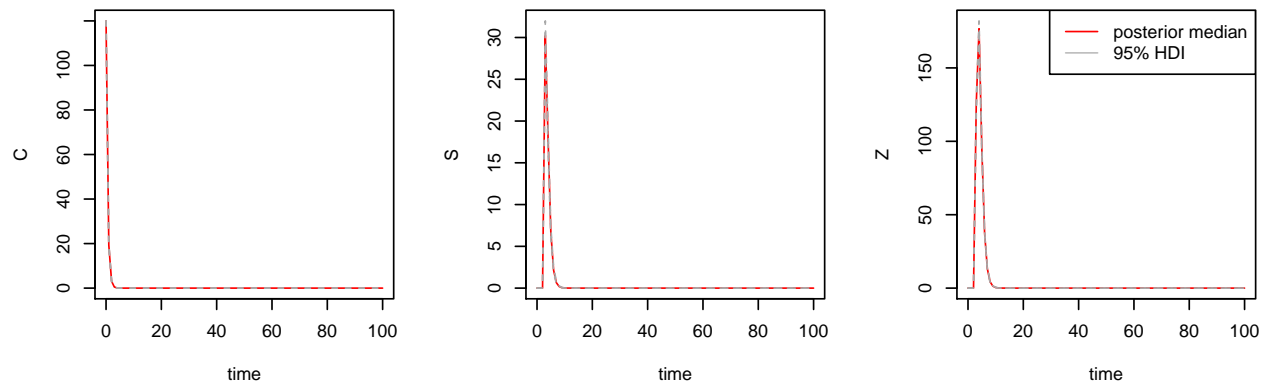
```
## sr      1.4036 0.09551 0.004271      0.032267
## fs      0.7580 0.03489 0.001560      0.009139
## ds      1.2317 0.08093 0.003619      0.013866
## muz     0.4621 0.05248 0.002347      0.010313
## eta    14.5560 0.68953 0.030837      0.168212
## Tmin    2.4075 0.03914 0.001750      0.006410
##
## 2. Quantiles for each variable:
##
##          2.5%    25%    50%    75%    97.5%
## sr      1.2953  1.3413  1.3789  1.4442  1.6346
## fs      0.7134  0.7443  0.7678  0.7778  0.7923
## ds      1.0985  1.1961  1.2482  1.2634  1.2939
## muz     0.3811  0.4372  0.4621  0.4874  0.5084
## eta    13.7685 14.2314 14.6550 14.9626 15.3391
## Tmin    2.3732  2.3870  2.4046  2.4160  2.4424
```

We simulate DE model trajectories from the posterior and calculate the HPD interval for the deterministic part of the model.

```
post_traj <- post_sim(dede_rev, n=20, times=0:100, burnin=burnin, output = 'all')
```

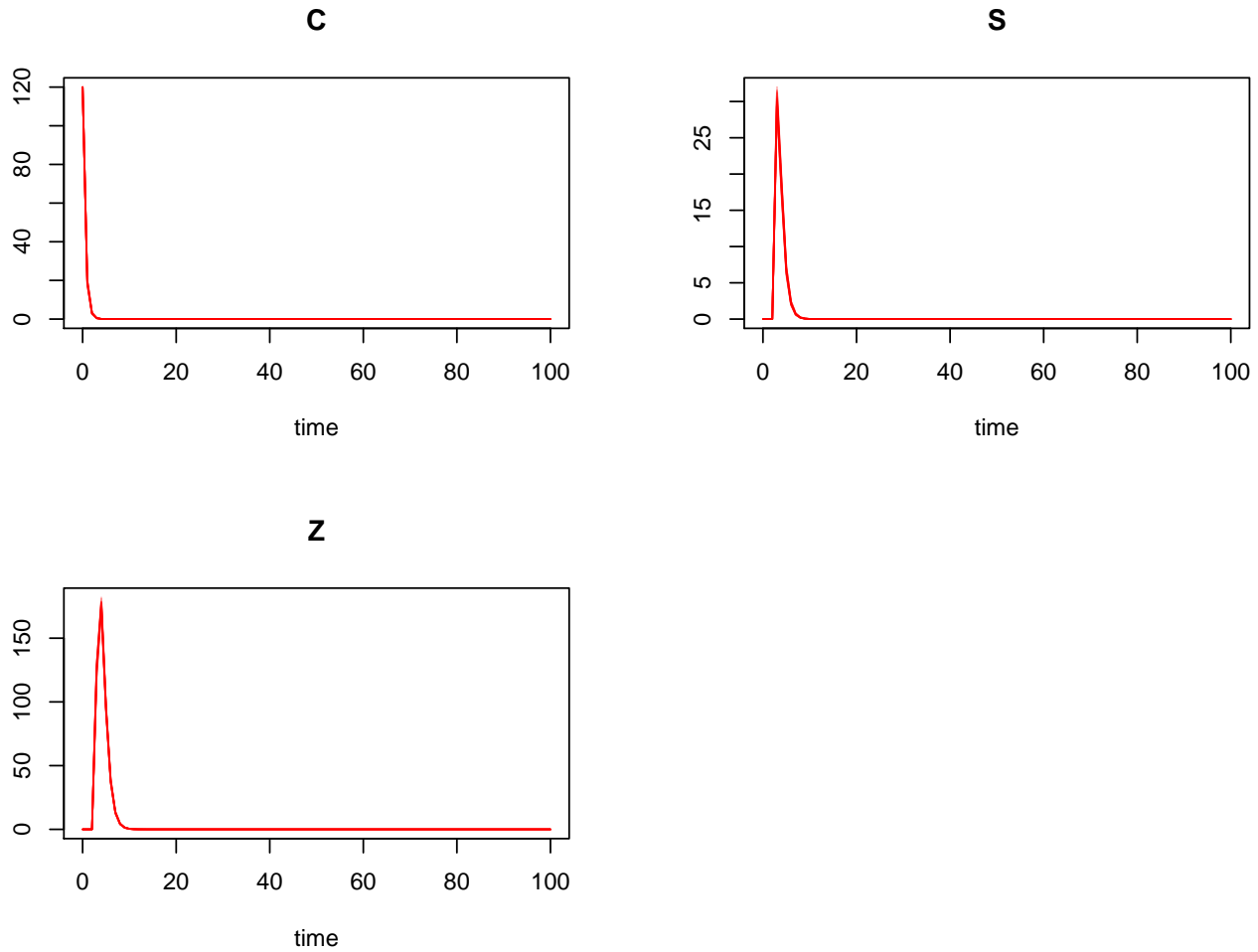
We can visualise the median posterior trajectory and the associated highest posterior density interval using

```
#median and HDI
par(mfrow=c(1,3))
plot(post_traj, plot.type = "medianHDI", auto.layout = FALSE)
legend("topright", legend=c("posterior median", "95% HDI"), lty=1, col=c("red","grey"))
```



Alternatively we can plot an ensemble of posterior trajectories

```
plot(post_traj, plot.type = "ensemble", col = "#FF000040")
```



## References

- Rosenblum, Erica Bree, Jamie Voyles, Thomas J Poorten, and Jason E Stajich. 2010. "The Deadly Chytrid Fungus: A Story of an Emerging Pathogen." *PLoS Pathogens* 6 (1): 1–3. doi:10.1371/journal.ppat.1000550.
- Soetaert, KER, Thomas Petzoldt, and R Woodrow Setzer. 2010. "Solving Differential Equations in R: Package DeSolve." *Journal of Statistical Software* 33 (9): 1–25.
- Voyles, Jamie, Leah R Johnson, Cheryl J Briggs, Scott D Cashins, Ross A Alford, Lee Berger, Lee F Skerratt, Rick Speare, and Erica Bree Rosenblum. 2012. "Temperature Alters Reproductive Life History Patterns in *Batrachochytrium Dendrobatidis*, a Lethal Pathogen Associated with the Global Loss of Amphibians." *Ecology and Evolution* 2 (9). Wiley Online Library: 2241–9.