Speeding up parameter inference with compiled models

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Differential equation (DE) models in R are easy to implement and allow simple interactive development using readable code and access to `R`'s many high-level functions. This was part of our motivation to develop `deBInfer` as an R based inference package. However, numerically solving DE models specified as `R` functions is also relatively slow. The `deSolve` package also allows the evaluation of DE models that are defined in lower-level languages such as `C` and `FORTRAN`. These compiled models have the benefit of increased simulation speed. As the DE model is evaluated many times during the MCMC procedure, even moderate speed-ups from using compiled models can result in large absolute time savings.

We demonstrate the speed-up using an example from the `deSolve` documentation (Soetaert *et al.* 2010). Full details on the model specification can be found in Soetaert et al. (2009) which can be displayed with the command `vignette("compiledCode")`. Further details on the set up of the `deBInfer` inference procedure are described in Boersch-Supan et al. (2016) and annotated examples are available in the vignettes `vignette("logistic_ode_example")` and `vignette("vignette_chytrid_dede_example")`.

1 Specifying the ODE model

Following Soetaert et al. (2009), we use the following simple ODE:

$$\frac{dy_1}{dt} = -k_1 \cdot y_1 + k_2 \cdot y_2 \cdot y_3$$
$$\frac{dy_2}{dt} = k_1 \cdot y_1 - k_2 \cdot y_2 \cdot y_3 - k_3 \cdot y_2 \cdot y_2$$
$$\frac{dy_3}{dt} = k_3 \cdot y_2 \cdot y_2$$

where y_1, y_2 and y_3 are state variables, and k_1, k_2 and k_3 are parameters.

1.1 ODE model implementation in R

We implement this model as an `R` function:

```r
modelR <- function(t, Y, parameters) {
  with (as.list(parameters),{

    dy1 = -k1*Y[1] + k2*Y[2]*Y[3]
    dy3 = k3*Y[2]*Y[2]
    dy2 = -dy1 - dy3

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

And also specify the Jacobian ($\frac{\partial y'}{\partial y}$) for it:

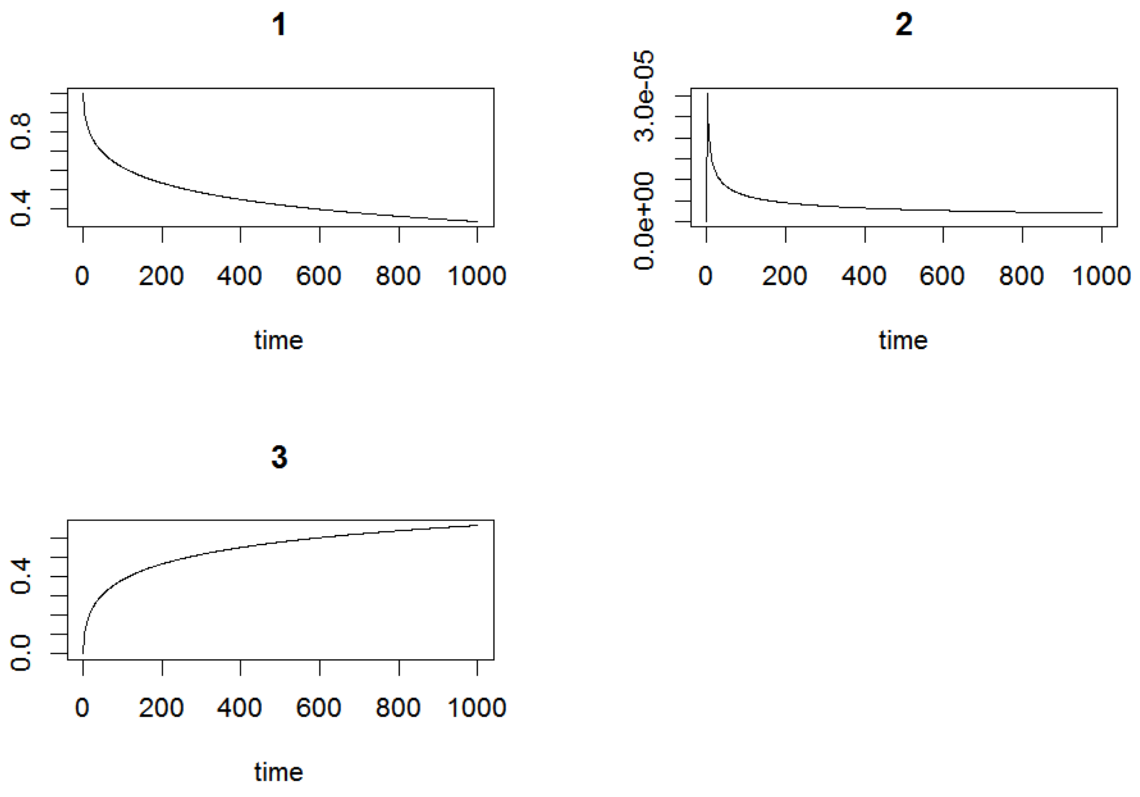
```
jacR <- function (t, Y, parameters) {
  with (as.list(parameters),{

    PD[1,1] <- -k1
    PD[1,2] <- k2*Y[3]
    PD[1,3] <- k2*Y[2]
    PD[2,1] <- k1
    PD[2,3] <- -PD[1,3]
    PD[3,2] <- k3*Y[2]
    PD[2,2] <- -PD[1,2] - PD[3,2]

    return(PD)
  })
}
```

This model can then be run as follows:

```
library(deSolve)
parms <- c(k1 = 0.04, k2 = 1e4, k3=3e7)
Y     <- c(1.0, 0.0, 0.0)
times <- seq(0, 0.1*10^4, length.out = 1000)
PD    <- matrix(nrow = 3, ncol = 3, data = 0)
outR   <- ode(Y, times, modelR, parms = parms, jacfunc = jacR)
plot(outR)
```



1.2 ODE model implementation in C

To create compiled models (dynamic-link libraries (.dll) on Windows or shared objects (.so) on other systems) a recent version of the GNU compiler suite is required. This is usually the case for Linux systems. Windows users can install the required toolchain by following the instructions on [https://cran.r-project.org/bin/windows/Rtools/]. OSX users need to download and install an appropriate version of Xcode from the Apple developer website [https://developer.apple.com/] or the OSX App Store.

The call to the derivative and Jacobian function is more complex for compiled code compared to `R`-code, because it has to comply with the interface needed by the integrator. The requirements for this are detailed in Soetaert et al. (2009). A `C` implementation of the example model is found below.

```
/* file mymod.c */
#include <R.h>
static double parms[3];
#define k1 parms[0]
#define k2 parms[1]
#define k3 parms[2]

/* initializer  */
void initmod(void (* odeparms)(int *, double *))
{
    int N=3;
    odeparms(&N, parms);
}

/* Derivatives and 1 output variable */
void derivs (int *neq, double *t, double *y, double *ydot,
             double *yout, int *ip)
{
    if (ip[0] <1) error("nout should be at least 1");
    ydot[0] = -k1*y[0] + k2*y[1]*y[2];
    ydot[2] = k3 * y[1]*y[1];
    ydot[1] = -ydot[0]-ydot[2];

    yout[0] = y[0]+y[1]+y[2];
}

/* The Jacobian matrix */
void jac(int *neq, double *t, double *y, int *ml, int *mu,
           double *pd, int *nrowpd, double *yout, int *ip)
{
  pd[0]                 = -k1;
  pd[1]                 = k1;
  pd[2]                 = 0.0;
  pd[(*nrowpd)]         = k2*y[2];
  pd[(*nrowpd) + 1]     = -k2*y[2] - 2*k3*y[1];
  pd[(*nrowpd) + 2]     = 2*k3*y[1];
  pd[(*nrowpd)*2]       = k2*y[1];
  pd[2*(*nrowpd) + 1] = -k2 * y[1];
  pd[2*(*nrowpd) + 2] = 0.0;
}
/* END file mymod.c */
```

2 Running ODE models implemented in compiled code

To run the C implementation of the model it must first be compiled. This can be done using the R system statement

```
system("R CMD SHLIB mymod.c")
```

which will create the file mymod.dll on Windows, or mymod.so on other platforms.

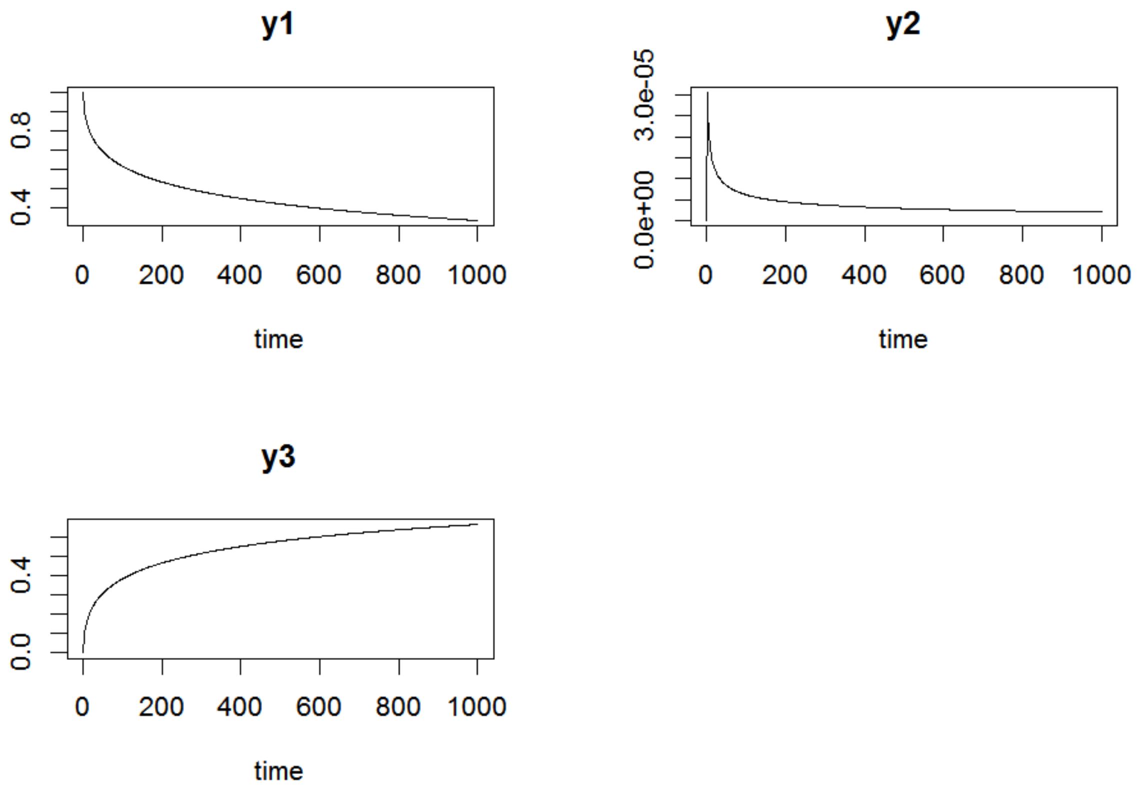
We can then load the compiled model with

```
dyn.load(paste("mymod", .Platform$dynlib.ext, sep = ""))
```

The model can now be run as follows:

```
parms <- c(k1 = 0.04, k2 = 1e4, k3=3e7)
Y     <- c(y1 = 1.0, y2 = 0.0, y3 = 0.0)
times <- seq(0, 0.1*10^4, length.out = 1000)

out <- ode(Y, times, func = "derivs", parms = parms,
           jacfunc = "jac", dllname = "mymod",
           initfunc = "initmod", nout = 1, outnames = "Sum")
plot(out, which = 1:3)
```



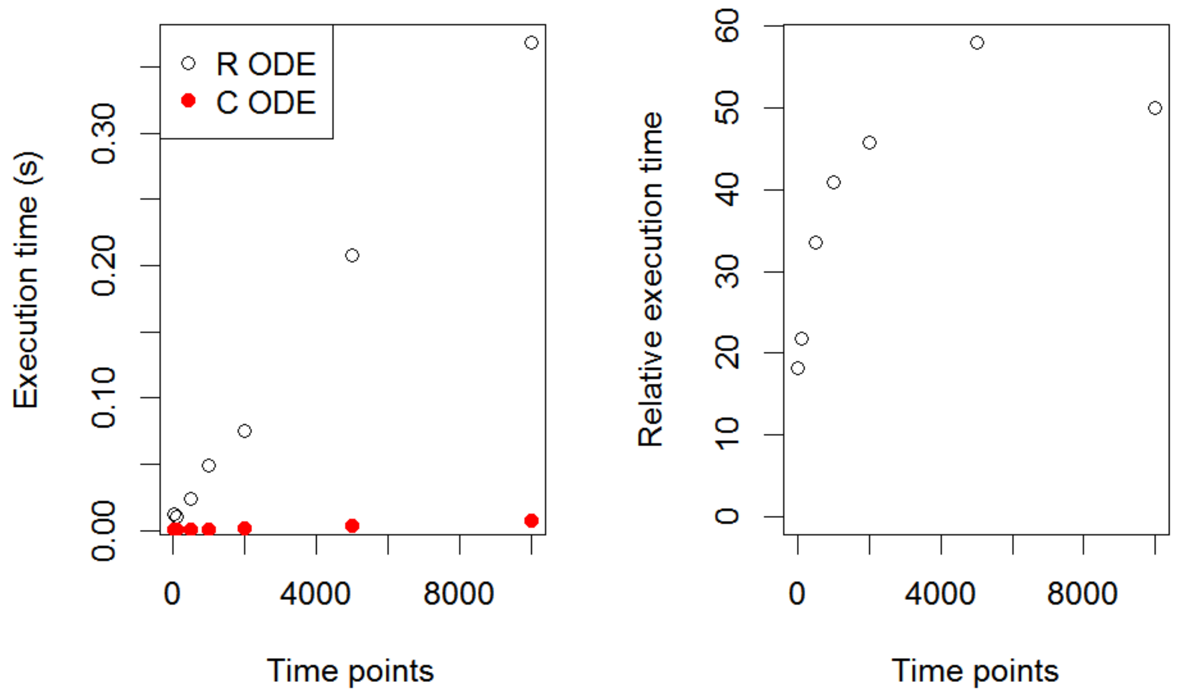
We can determine the speed improvement as a function of desired output time points using the microbenchmark package

```r
timepoints <- c(10,100, 500, 1000,2000, 5000, 10000)

solve_time <- lapply(timepoints, function(x){
                times <- seq(0, 0.1*10^4, length.out = x)
                comp <- microbenchmark::microbenchmark(
                  C = ode(Y, times, func = "derivs", parms = parms,
                           jacfunc = "jac", dllname = "mymod",
                           initfunc = "initmod", nout = 1, outnames = "Sum"),
                  R = ode(Y, times, modelR, parms = parms, jacfunc = jacR), times=10
                  )
                  return(comp)
                  }
                )

#saveRDS(solve_time, "examples/Soetaert-r-vs-c-solve_time.RDS")

solve_speedup <- sapply(solve_time,
                        function(x)mean(x$time[x$expr=="R"]/x$time[x$expr=="C"]))
solve_R <- sapply(solve_time, function(x)mean(x$time[x$expr=="R"]/1e9))
solve_C <- sapply(solve_time, function(x)mean(x$time[x$expr=="C"]/1e9))
#pdf("examples/c-vs-r-solve.pdf")
par(mfrow=c(1,2))
plot(timepoints, solve_R, type="p", ylab = "Execution time (s)", xlab = "Time points")
points(timepoints, solve_C, col="red", type="p", pch=c(16))
legend("topleft", legend = c("R ODE", "C ODE"), pch = c(1,16), col= c("black", "red"))
plot(rep(timepoints, each=1), solve_speedup, type="p", ylab = "Relative execution time"
     , xlab = "Time points", ylim = c(0,max(solve_speedup)))
```



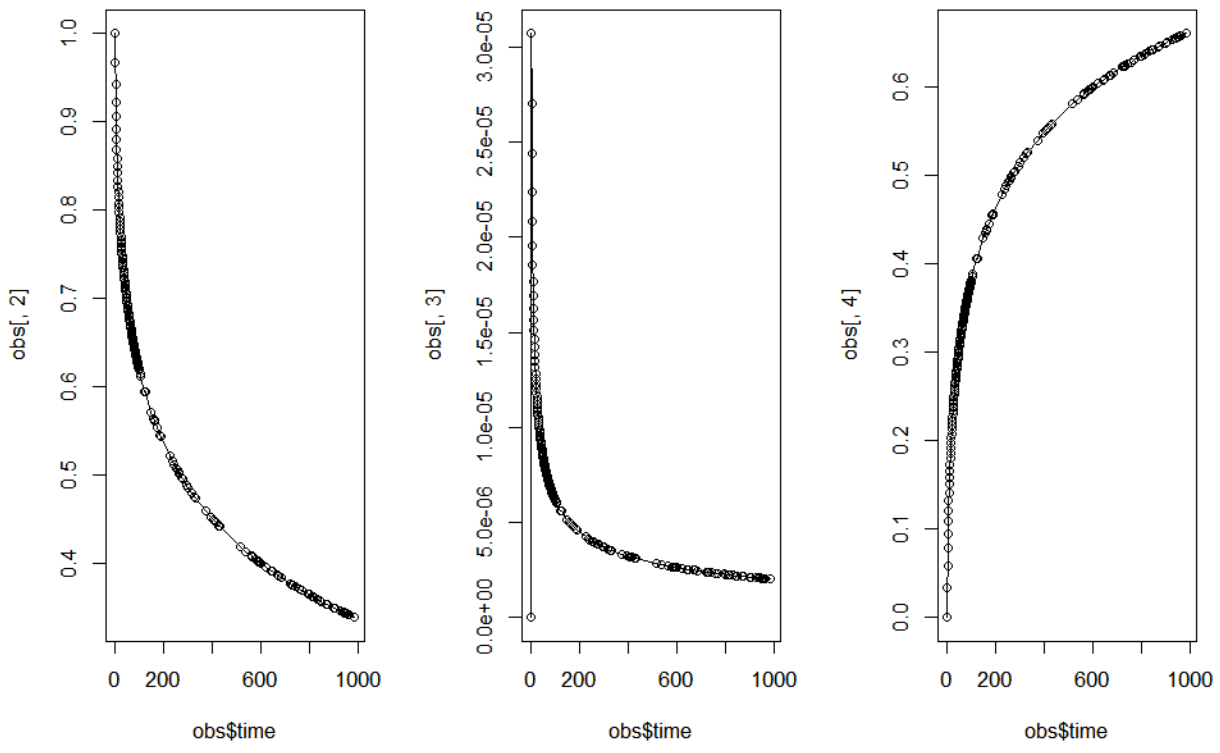
```r
#dev.off()
```

which shows us that the `C` version of the models is solved 18-58 times faster than the `R` version.

3 Conducting inference with compiled models

We can now simulate a dataset to demonstrate the inference procedure:

```r
set.seed(143)
#force include the first time-point (t=0)
obs <- as.data.frame(outR[c(1:100,runif(100, 0, nrow(outR))),])
obs <- obs[order(obs$time),]
par(mfrow=c(1,3))
plot(obs$time, obs[,2], type='o')
plot(obs$time, obs[,3], type='o')
plot(obs$time, obs[,4], type='o')
```



4 Defining an observation model and parameters for inference

For simplicity we assume a normal log-likelihood for these data

$$\ell(\mathcal{Y}|\boldsymbol{\theta}) = \sum_i \sum_t \ln\left(\frac{1}{\sigma_{obs}\sqrt{2\pi}} \exp\left(-\frac{(\tilde{y}_{t,i} - (y_{t,i})^2}{2\sigma_{obs}^2}\right)\right) \tag{1}$$

where $\tilde{y}_{t,i}$ are the observations, and $y_{t,i}$ are the predictions of the DE model given the current MCMC sample of the parameters $\boldsymbol{\theta}$.

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

  llik.y1 <- sum(dnorm(obs[,2], mean = sim.data[,2], sd = samp[['sd.y1']], log = TRUE))
  llik.y2 <- sum(dnorm(obs[,3], mean = sim.data[,3], sd = samp[['sd.y2']], log = TRUE))
  llik.y3 <- sum(dnorm(obs[,4], mean = sim.data[,4], sd = samp[['sd.y3']], log = TRUE))
  return(llik.y1 + llik.y2 + llik.y3)
}
```

We declare the DE model parameters and their associated priors and MCMC parameters. Note that we are using the asymmetric uniform proposal distribution $\mathcal{U}(\frac{a}{b}\theta^{(k)}, \frac{b}{a}\theta^{(k)})$ for the variance parameters (`samp.type="rw-unif"`), as this ensures strictly positive proposals.

```r
library(deBInfer)
k1 <- debinfer_par(name = "k1", var.type = "de", fixed = FALSE,
                value = 0.05, prior = "lnorm", hypers = list(meanlog = 0, sdlog = 1),
                 prop.var = c(998,1000), samp.type = "rw-unif")

k2 <- debinfer_par(name = "k2", var.type = "de", fixed = FALSE,
                value = 8000, prior = "norm", hypers = list(mean = 5000, sd = 1000),
                prop.var = 500, samp.type="rw")
k3 <- debinfer_par(name = "k3", var.type = "de", fixed = FALSE,
                value = 3e7, prior = "norm", hypers = list(mean = 1e7, sd = 5e6),
                prop.var = 5e7, samp.type="rw")

sd.y1 <- debinfer_par(name = "sd.y1", var.type = "obs", fixed = FALSE,
                value = 0.05, prior = "lnorm", hypers = list(meanlog = 0, sdlog = 1),
                prop.var = c(3,4), samp.type = "rw-unif")
sd.y2 <- debinfer_par(name = "sd.y2", var.type = "obs", fixed = FALSE,
                value = 0.05, prior = "lnorm", hypers = list(meanlog = 0, sdlog = 1),
                prop.var = c(3,4), samp.type = "rw-unif")
sd.y3 <- debinfer_par(name = "sd.y3", var.type = "obs", fixed = FALSE,
                value = 0.05, prior = "lnorm", hypers = list(meanlog = 0, sdlog = 1),
                prop.var = c(3,4), samp.type = "rw-unif")


#Lastly, we provide initial values for the DE:

y1 <- debinfer_par(name = "y1", var.type = "init", fixed = TRUE, value = 1)
y2 <- debinfer_par(name = "y2", var.type = "init", fixed = TRUE, value = 0)
y3 <- debinfer_par(name = "y3", var.type = "init", fixed = TRUE, value = 0)
```

The declared parameters are then collated using the `setup_debinfer` function. Note that for models with more than one state variable, **the initial values must be entered in the same order, as they are specified in the DE model function**, as the solver matches these values by position, rather than by name. More details can be found in `?deSolve::ode`. The remaining parameters can be entered in any order for the `R` based inference, **but are matched by position in the compiled model**.

```r
mcmc.pars <- setup_debinfer(k1, k2, k3, sd.y1, sd.y2, sd.y3, y1, y2, y3)
```

5 Conduct inference

Finally we use deBInfer to estimate the parameters of the original model

```r
# do inference with deBInfer
  # MCMC iterations
iter <- 1000
  # inference call
Rt <- system.time(mcmc_samples <- de_mcmc(N = iter, data = obs, de.model = modelR,
                          obs.model = obs_model, all.params = mcmc.pars,
                          Tmax = max(obs$time), data.times = obs$time, cnt = 500,
                          plot = FALSE, solver = "ode", verbose.mcmc = FALSE))
```

```
## Order of initial conditions is  y1, y2, y3
## initial posterior probability = 568.058099497889
```

```
Ct <- system.time(mcmc_samplesC <- de_mcmc(N = iter, data = obs, de.model = "derivs",
          jacfunc = "jac", dllname = "mymod",
          initfunc = "initmod", nout = 1, outnames = "Sum",
                         obs.model = obs_model, all.params = mcmc.pars,
                         Tmax = max(obs$time), data.times = obs$time, cnt = 1250,
                         plot = FALSE, solver = "ode", verbose.mcmc = FALSE))
```

```
## Order of initial conditions is  y1, y2, y3
## initial posterior probability = 568.058099497889
```

```
print(Rt)
```

```
##    user  system elapsed
##   45.32    0.00   45.42
```

```
print(Ct)
```

```
##    user  system elapsed
##    7.81    0.00    7.88
```

```
#coda::rejectionRate(mcmc_samplesC$samples)
#plot(mcmc_samplesC)
```

and simulate posterior trajectories.

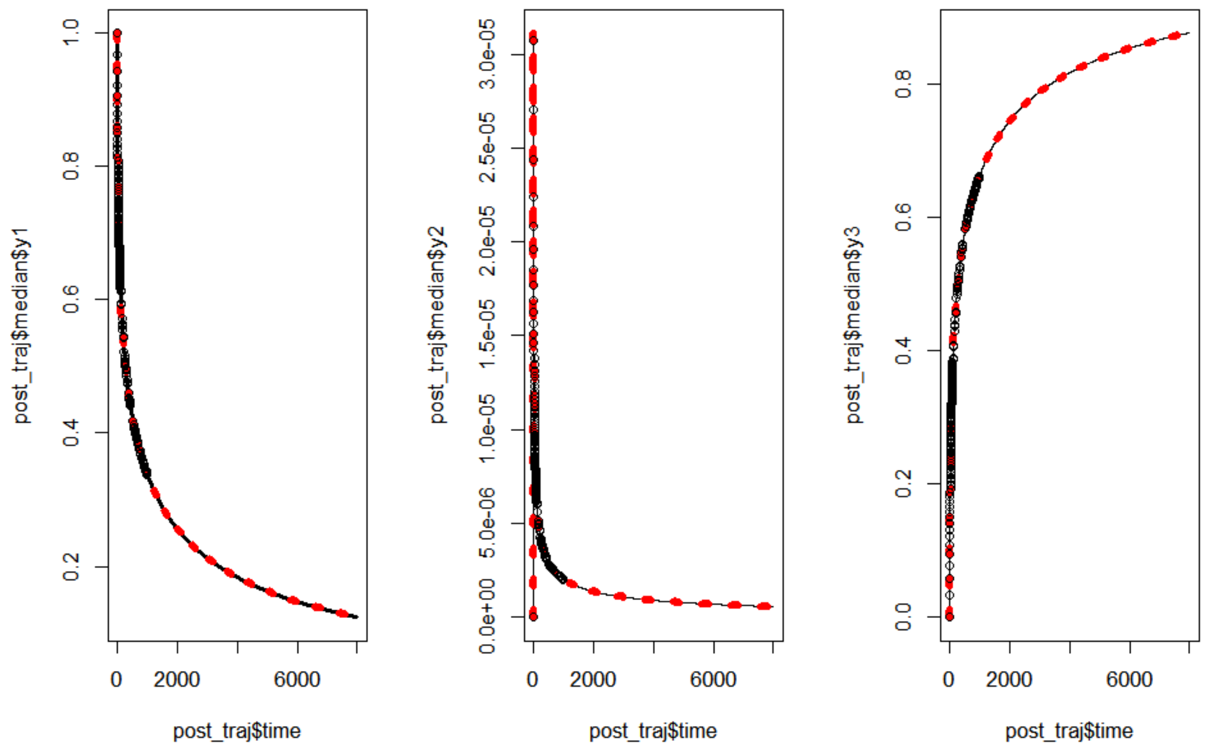
```
system.time(post_traj <- post_sim(mcmc_samples, n=100, times=0:8000, burnin=100,
                                  output = 'all', prob = 0.95))
```

```
##    user  system elapsed
##   35.75    0.21   36.17
```

```
system.time(post_trajC <- post_sim(mcmc_samplesC, n=100, times=0:8000, burnin=100,
                                   output = 'all', prob = 0.95, jacfunc = "jac",
                                   dllname = "mymod",initfunc = "initmod", nout = 1,
                                   outnames = "Sum"))
```

```
##    user  system elapsed
##    3.72    0.17    3.89
```

```
par(mfrow=c(1,3))
plot(post_traj$time, post_traj$median$y1, type='l',lwd=2)
lines(post_trajC$time, post_trajC$median$y1, col="red", lty=3, lwd=4)
points(obs$time, obs[,2])
plot(post_traj$time, post_traj$median$y2, type='l')
lines(post_trajC$time, post_trajC$median$y2, col="red", lty=3, lwd=4)
points(obs$time, obs[,3])
plot(post_traj$time, post_traj$median$y3, type='l')
lines(post_trajC$time, post_trajC$median$y3, col="red", lty=3, lwd=4)
points(obs$time, obs[,4])
```



We can see that inference and posterior simulations using the compiled model are substantially faster. This speed up is consistent across a range of MCMC iterations:

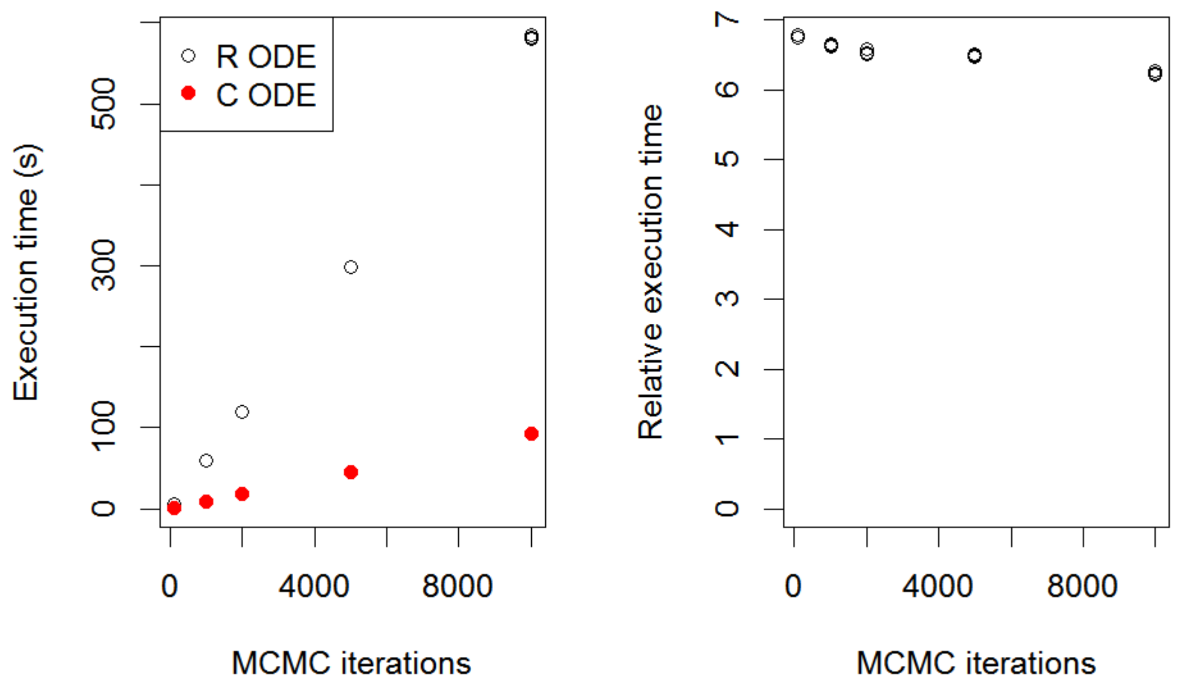
```
iter_reps <- rep(c(100,1000,2000,5000,10000),3)
timings <- matrix(nrow=length(iter_reps),ncol=2)

for (i in seq_along(iter_reps)){

  timings[i,1] <- system.time(mcmc_samples <- de_mcmc(N = iter_reps[i], data = obs,
                          de.model = modelR,
                          obs.model = obs_model, all.params = mcmc.pars,
                          Tmax = max(obs$time), data.times = obs$time, cnt = 500,
                          plot = FALSE, solver = "ode", verbose.mcmc = FALSE))[3]
  timings[i,2] <- system.time(mcmc_samplesC <- de_mcmc(N = iter_reps[i], data = obs,
                          de.model = "derivs",
                          jacfunc = "jac", dllname = "mymod",
                          initfunc = "initmod", nout = 1, outnames = "Sum",
                          obs.model = obs_model, all.params = mcmc.pars,
                          Tmax = max(obs$time), data.times = obs$time, cnt = 1250,
                          plot = FALSE, solver = "ode", verbose.mcmc = FALSE))[3]
}
#saveRDS(timings, "examples/Soetaert-r-vs-c-timings.RDS")
```

```
iter_reps <- rep(c(100,1000,2000,5000,10000),3)
if(!exists("timings")) timings <- readRDS("Soetaert-r-vs-c-timings.RDS")
#pdf("examples/c-vs-r-iters.pdf")
```

```r
par(mfrow=c(1,2))
plot(iter_reps, timings[,1], ylim=c(0, max(timings[,1])), type="p",
     ylab = "Execution time (s)", xlab = "MCMC iterations")
points(iter_reps, timings[,2], col="red", type="p", pch=c(1,16))
legend("topleft", legend = c("R ODE", "C ODE"), pch = c(1,16), col= c("black", "red"))
plot(iter_reps, timings[,1]/timings[,2], ylim=c(0, max(timings[,1]/timings[,2])), type="p",
     ylab = "Relative execution time", xlab = "MCMC iterations")
```



```r
#dev.off()
```

Boersch-Supan, P., Ryan, S. & Johnson, L. (2016). deBinfer: Bayesian inference for dynamical models of biological systems. *arXiv*, **1605.00021**.

Soetaert, K., Petzoldt, T. & Setzer, R.W. (2009). *R package desolve, writing code in compiled languages.*

Soetaert, K., Petzoldt, T. & Setzer, R.W. (2010). Solving differential equations in R: Package deSolve. *Journal of Statistical Software*, **33**, 1–25.