Suggested workflow for epidemiological modeling and inference

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Summary I

1. **Data Preparation and Model Specification**
   - **Data Initialization**: Visualize the initial data to get a sense of the disease outbreak dynamics. (*Simulation P22*)
   - **Model Definition**: Implement the defined SIR model in `pomp`
     - Set up a stochastic SIR (Susceptible, Infected, Recovered) model using custom C snippets for state transitions and measurements. (*Simulation P36*)
     - Specify the measurement, process, and initialization functions along with model parameters. (*Simulation P38-40*)
2. **Preliminary Analysis**
   - **Simulation and Visualization**: Simulate the SIR model to visualize potential outcomes and compare to data. (*Simulation P44*)
   - **Likelihood Estimation**: Evaluate the likelihood and Effective Sample Size of the initial parameter estimates using particle filtering. (*likelihood P28-29*)

Summary II

3. **Local Optimization**
    - **Iterated Filtering for Local Maximum**: Apply iterated filtering to find a local maximum near the initial guesses. (*Iterated filtering P27*)
    - **Diagnostics and Visualization**: Diagnose the iterated filtering process and visualize parameter traces to assess convergence. (*Iterated filtering P29,33,34*)
4. **Global Optimization**
    - **Set Up for Global Search**: Define a parameter space for global optimization. (*Iterated filtering P38*)
    - **Global Search Execution**: Conduct global optimization using multiple starting points to ensure robustness of the findings. (*Iterated filtering P39*)
    - **Result Compilation**: Compile and compare results from global searches, focusing on the best parameter estimates. (*Iterated filtering P42,45*)

Summary III

5. **Profile Likelihood Estimation**
    - **Parameter Profiling**: For each parameter, perform profiling to map the likelihood landscape and establish confidence intervals. (*Iterated filtering P48,49,52*)
    - **Visualization of Profile Likelihoods**: Visualize the profile likelihoods to understand parameter sensitivity and uncertainty. (*Iterated filtering P53, 57, 60*)
6. **Final Model Evaluation**
    - **Model Predictions**: Use the best-fitting parameters to simulate the model outcomes and compare these against observed data. (*Iterated filtering P87*)
    - **Visualization of Predictions**: Create visualizations to compare the model predictions with actual data, highlighting the prediction intervals. (*Iterated filtering P88*)
7. **Documentation and Storage**
    - **Record-Keeping**: All intermediate and final results should be stored in CSV files for further analysis or reproducibility of the study.

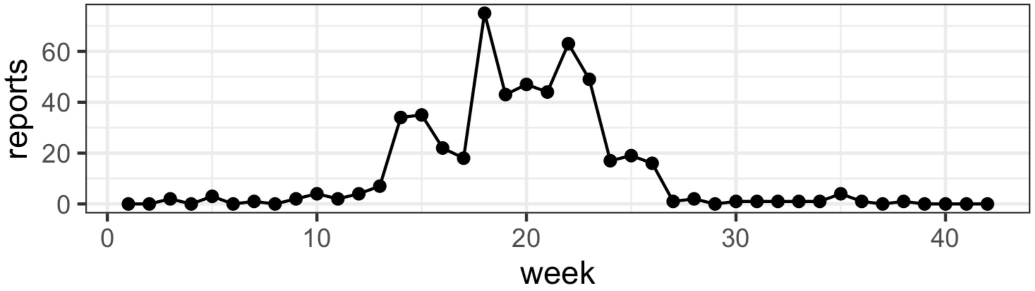
Measle example: Data initialization I

```r
library(tidyverse)
read_csv("Measles_Consett_1948.csv") |>
  select(week,reports=cases) |>
  filter(week<=42) -> meas
meas |> as.data.frame() |> head(n=3)
```

```
 week reports
    1       0
    2       0
    3       2
```

Measle example: Data initialization II

```
meas |>
  ggplot(aes(x=week,y=reports)) +
  geom_line() + geom_point()
```



Measle example: stochastic SIR model in pomp I

```
sir_stoch <- Csnippet("
  double dN_SI = rbinom(S,1-exp(-Beta*I/N*dt));
  double dN_IR = rbinom(I,1-exp(-Gamma*dt));
  S -= dN_SI; I += dN_SI - dN_IR;
  R += dN_IR; H += dN_IR;"
)

sir_init <- Csnippet("
  S = nearbyint(Eta*N);
  I = 1;
  R = nearbyint((1-Eta)*N);
  H = 0;"
)
```

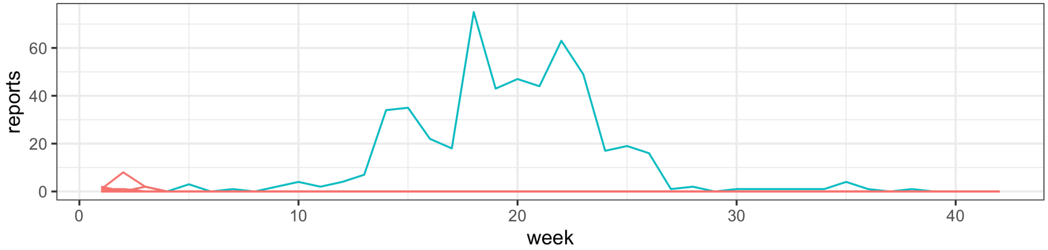
Measle example: stochastic SIR model in pomp II

```
dmeas <- Csnippet("lik = dnbinom_mu(reports,k,Rho*H,give_log);")
rmeas <- Csnippet("reports = rnbinom_mu(k,Rho*H);")

meas |>
  pomp(
    times="week",t0=0,
    rprocess=euler(sir_stoch,delta.t=1/7),
    rinit=sir_init, rmeasure=rmeas,
    dmeasure=dmeas, accumvars="H",
    statenames=c("S","I","R","H"),
    paramnames=c("Beta","Gamma","Eta","Rho","k","N"),
    params=c(Beta=15,Gamma=2,Rho=0.5,k=10,Eta=0.06,N=38000)
  ) -> measSIR
```

Preliminary analysis: simulation and exploration

```r
measSIR |>
  simulate(nsim=20,format="data.frame",include.data=TRUE) |>
  ggplot(aes(x=week,y=reports,group=.id,color=.id=="data")) +
  geom_line() + guides(color="none")
```



Preliminary analysis: likelihood and ess I

Evaluate the likelihood and Effective Sample Size (ESS) of the initial parameter estimates using particle filtering

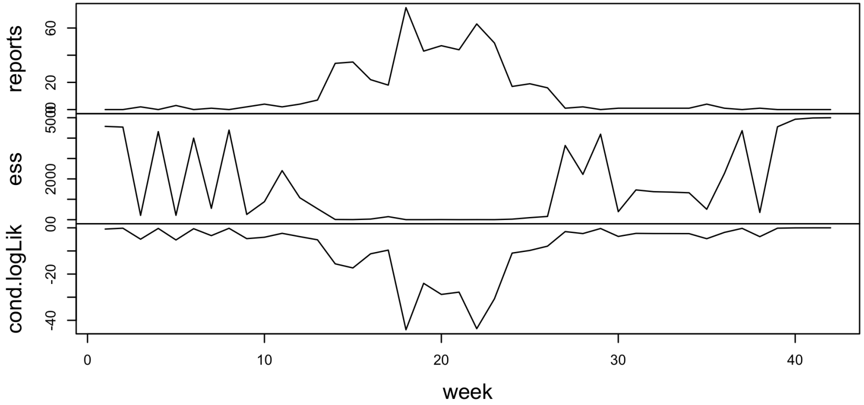
```
pf <- measSIR |> pfilter(Np=5000)
min(pf@eff.sample.size)
```

```
[1] 1.103539
```

ESS refers to the number of particles that effectively contribute to the approximation of the posterior distribution.

```
plot(pf)
```

Preliminary analysis: likelihood and ess II



Preliminary analysis: likelihood and ess III

Use repeated particle filtering to refine estimates

```r
foreach(i=1:10,.combine=c,
  .options.future=list(seed=TRUE)) %dofuture% {
  measSIR |> pfilter(Np=5000)
} -> pf
pf |> logLik() |> logmeanexp(se=TRUE) -> L_pf
L_pf
```

```
      est          se
-269.01842   19.98634
```

Preliminary analysis: likelihood and ess IV

Then we get likelihood at a single point. Store this point, together with the estimated likelihood and SE:

```r
pf[[1]] |> coef() |> bind_rows() |>
  bind_cols(loglik=L_pf[1],loglik.se=L_pf[2]) |>
  write_csv("measles_params.csv")
```

Local optimization I

- Apply iterated filtering to find a local maximum near the initial guesses

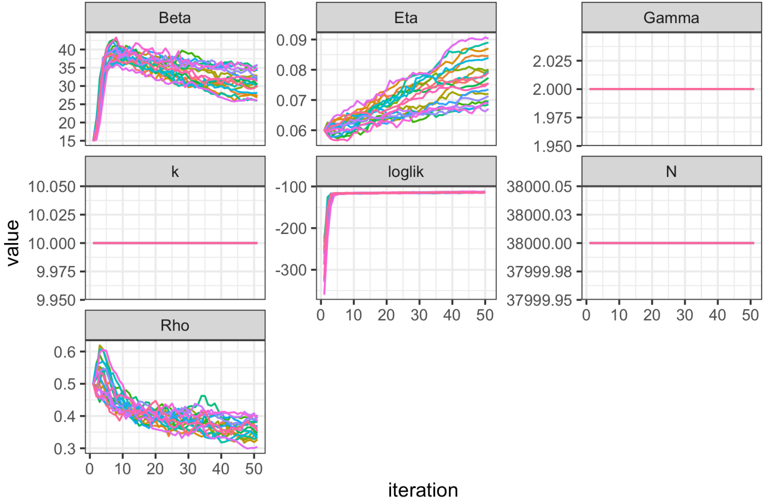
```r
foreach(i=1:20,.combine=c,
  .options.future=list(seed=482947940)) %dofuture% {
  measSIR |>
    mif2(
      Np=2000, Nmif=50, cooling.fraction.50=0.5,
      rw.sd=rw_sd(Beta=0.02, Rho=0.02, Eta=ivp(0.02)),
      partrans=parameter_trans(
        log="Beta",logit=c("Rho","Eta")
      ),
      paramnames=c("Beta","Rho","Eta")
    )
} -> mifs_local
```

Local optimization II

- Diagnostics and Visualization:

```r
mifs_local |>
  traces() |>
  melt() |>
  ggplot(aes(x=iteration,y=value,group=.L1,color=factor(.L1)))+
  geom_line()+
  guides(color="none")+
  facet_wrap(~name,scales="free_y")
```

Local optimization III



Local optimization IV

- evaluate the likelihood, together with a standard error

```
foreach(mf=mifs_local,.combine=rbind,
  .options.future=list(seed=900242057)
) %dofuture% {
  evals <- replicate(10, logLik(pfilter(mf,Np=5000)))
  ll <- logmeanexp(evals,se=TRUE)
  mf |> coef() |> bind_rows() |>
    bind_cols(loglik=ll[1],loglik.se=ll[2])
} -> results
```

```
results |> filter(loglik==max(loglik))
```

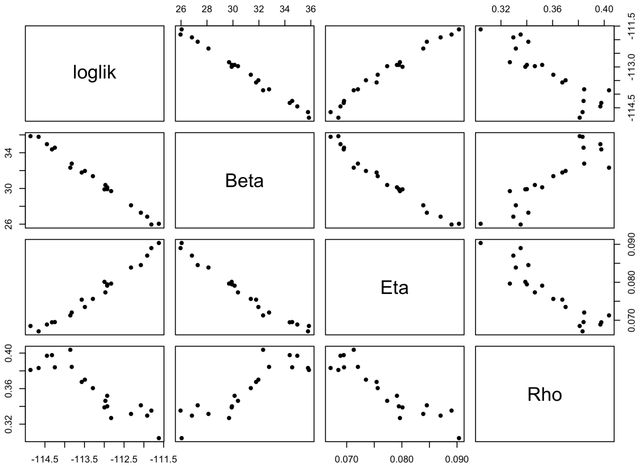
Local optimization V

```
# A tibble: 1 x 8
   Beta Gamma   Rho     k    Eta     N loglik loglik.se
  <dbl> <dbl> <dbl> <dbl>  <dbl> <dbl>  <dbl>     <dbl>
1  26.0     2 0.304    10 0.0904 38000  -112.    0.0630
```

- Generate likelihood surface

```
pairs(~loglik+Beta+Eta+Rho,data=results,pch=16)
```

Local optimization VI



Global optimization: setup I

1. Likelihood maximization from diverse starting points.
2. A large box in parameter space.
3. Expect to see stable conclusions with starting values drawn randomly from this box

```
set.seed(2062379496)
runif_design(
  lower=c(Beta=5,Rho=0.2,Eta=0),
  upper=c(Beta=80,Rho=0.9,Eta=1),
  nseq=400
) -> guesses
fixed_params <- c(N=38000, Gamma=2, k=10)
mf1 <- mifs_local[[1]]
```

Global optimization: global Search I

```
foreach(guess=iter(guesses,"row"), .combine=rbind,
  .options.future=list(seed=1270401374)
) %dofuture% {
  mf1 |>
    mif2(params=c(guess,fixed_params)) |>
    mif2(Nmif=100) -> mf
  replicate(
    10,
    mf |> pfilter(Np=5000) |> logLik()
  ) |>
    logmeanexp(se=TRUE) -> ll
  mf |> coef() |> bind_rows() |>
    bind_cols(loglik=ll[1],loglik.se=ll[2])
} -> results
```

Global optimization: global Search II

Then get the best result

```
results |> filter(loglik==max(loglik))
```

```
# A tibble: 1 x 8
   Beta    Rho   Eta     N Gamma     k loglik loglik.se
  <dbl>  <dbl> <dbl> <dbl> <dbl> <dbl>  <dbl>     <dbl>
1  3.96 0.0602 0.562 38000     2    10  -104.    0.0273
```

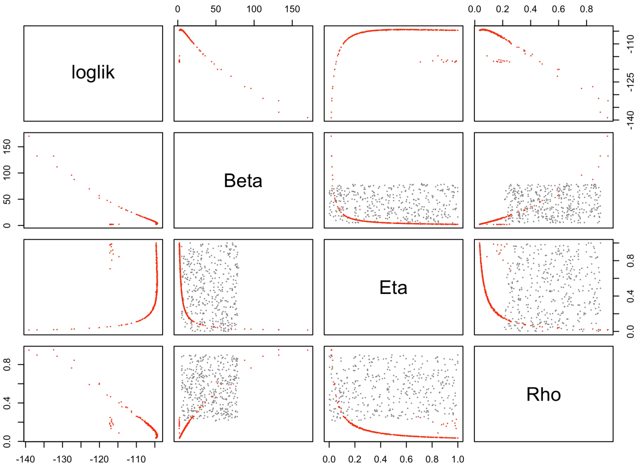
Global optimization: diagnostics and visualization I

Again, we attempt to visualize the global geometry of the likelihood surface using a scatterplot matrix. Then plot contains both the starting values (grey) and the IF2 estimates (red).

```
read_csv("measles_params.csv") |>
  filter(loglik>max(loglik)-50) |>
  bind_rows(guesses) |>
  mutate(type=if_else(is.na(loglik),"guess","result")) |>
  arrange(type) -> all
```

```
pairs(~loglik+Beta+Eta+Rho, data=all, pch=16, cex=0.3,
  col=ifelse(all$type=="guess",grey(0.5),"red"))
```

Global optimization: diagnostics and visualization II

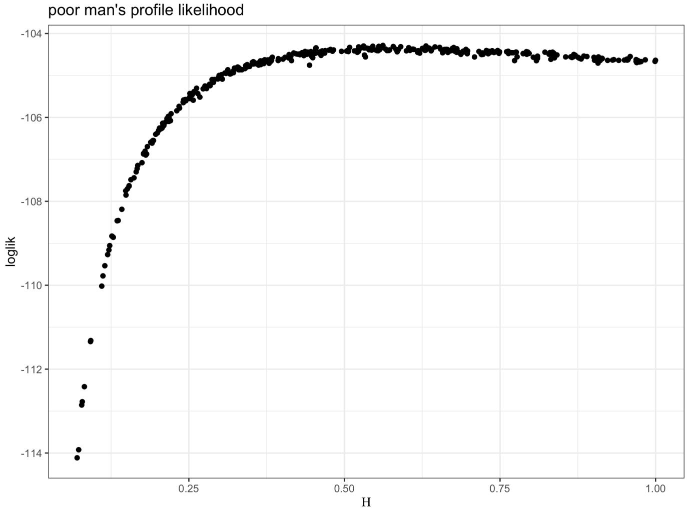


Global optimization: diagnostics and visualization III

The projections of the estimates give us 'poor mans profiles' ':

```r
all |>
  filter(type=="result") |>
  filter(loglik>max(loglik)-10) |>
  ggplot(aes(x=Eta,y=loglik))+
  geom_point()+
  labs(
    x=expression(Eta),
    title="poor man's profile likelihood"
  )
```

Global optimization: diagnostics and visualization IV



Profile: for the first parameter I

We first bound the uncertainty by putting a box around the highest-likelihood.

```
read_csv("measles_params.csv") |>
  filter(loglik>max(loglik)-20,loglik.se<2) |>
  sapply(range) -> box
box
```

```
          Beta Gamma        Rho  k        Eta     N
[1,]  1.824688     2 0.03405657 10 0.03628984 38000
[2,] 69.791919     2 0.60343428 10 0.99982180 38000
        loglik  loglik.se
[1,] -122.7423 0.01462075
[2,] -104.2847 0.56960880
```

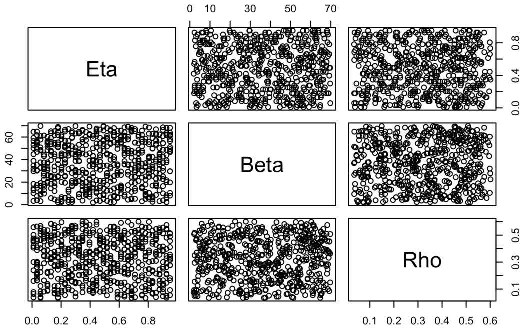
Profile: for the first parameter II

Within this box, we'll choose some random starting points

```r
freeze(seed=1196696958,
  profile_design(
    Eta=seq(0.01,0.95,length=40),
    lower=box[1,c("Beta","Rho")],
    upper=box[2,c("Beta","Rho")],
    nprof=15, type="runif"
  )) -> guesses
```

Profile: for the first parameter III

```
plot(guesses)
```



Profile: for the first parameter IV

Now, we'll start one independent sequence of iterated filtering operations from each of these points.

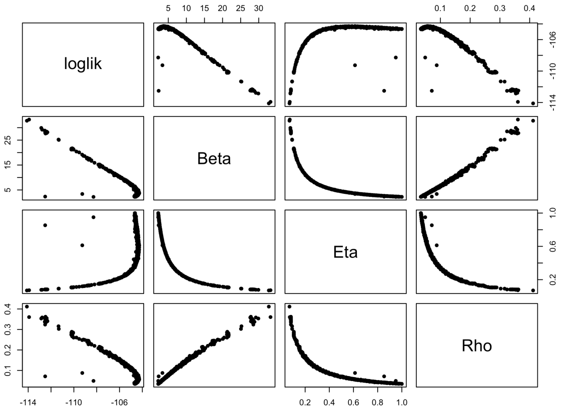
```r
foreach(guess=iter(guesses,"row"), .combine=rbind,
  .options.future=list(seed=830007657)
) %dofuture% {
  mf1 |>
    mif2(params=c(guess,fixed_params),
      rw.sd=rw_sd(Beta=0.02,Rho=0.02)) |>
    mif2(Nmif=100,cooling.fraction.50=0.3) -> mf
  replicate(10, mf |> pfilter(Np=5000) |> logLik()) |>
    logmeanexp(se=TRUE) -> ll
  mf |> coef() |> bind_rows() |>
    bind_cols(loglik=ll[1],loglik.se=ll[2])
} -> results
```

Profile visualization: for the first parameter I

```
read_csv("measles_params.csv") |>
  filter(loglik>max(loglik)-10) -> all

pairs(~loglik+Beta+Eta+Rho,data=all,pch=16)
```

Profile visualization: for the first parameter II

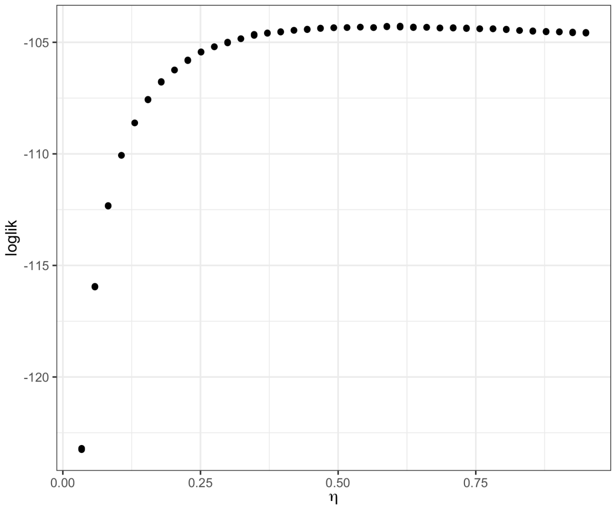


Profile visualization: for the first parameter III

Focusing on the top of the surface

```r
results |>
  filter(is.finite(loglik)) |>
  group_by(round(Eta,5)) |>
  filter(rank(-loglik)<3) |>
  ungroup() |>
  filter(loglik>max(loglik)-20) |>
  ggplot(aes(x=Eta,y=loglik))+
  geom_point() + xlab(expression(eta))
```

Profile visualization: for the first parameter IV



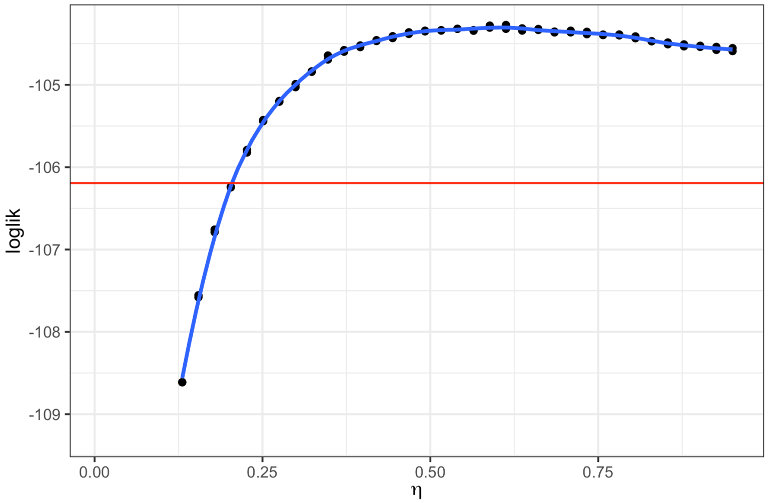
Profile visualization: for the first parameter V

Estimate η with 95% CI using these data

```r
maxloglik <- max(results$loglik,na.rm=TRUE)
ci.cutoff <- maxloglik-0.5*qchisq(df=1,p=0.95)

results |>
  filter(is.finite(loglik)) |>
  group_by(round(Eta,5)) |>
  filter(rank(-loglik)<3) |> ungroup() |>
  ggplot(aes(x=Eta,y=loglik))+
  geom_point() + xlab(expression(eta)) +
  geom_smooth(method="loess",span=0.25)+
  geom_hline(color="red",yintercept=ci.cutoff)+
  lims(y=maxloglik-c(5,0))
```

Profile visualization: for the first parameter VI



Profile visualization: for the first parameter VII

```
results |>
  filter(is.finite(loglik)) |>
  filter(loglik>max(loglik)-0.5*qchisq(df=1,p=0.95)) |>
  summarize(min=min(Eta),max=max(Eta)) -> Eta_ci
```

Then we know η is in the 0.23–0.95% range (95% CI).

Profile: for the later parameters I

For the next parameter, we can initialize the IF2 computations at points we have already established have high likelihoods.

```
read_csv("measles_params.csv") |>
  group_by(cut=round(Rho,2)) |>
  filter(rank(-loglik)<=10) |>
  ungroup() |>
  arrange(-loglik) |>
  select(-cut,-loglik,-loglik.se) -> guesses
```

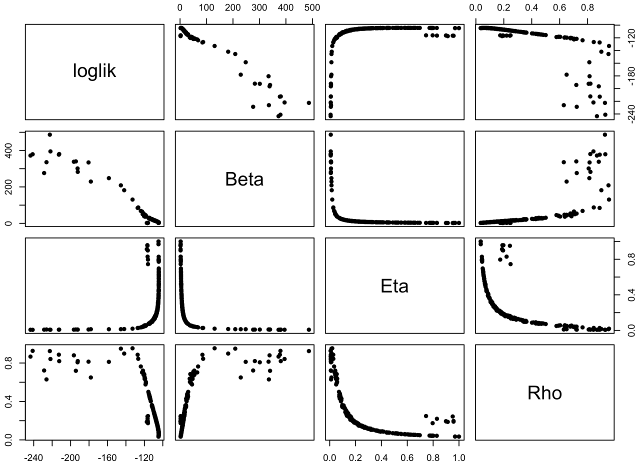
Profile: for the later parameters II

Then again, generate the profile likelihood

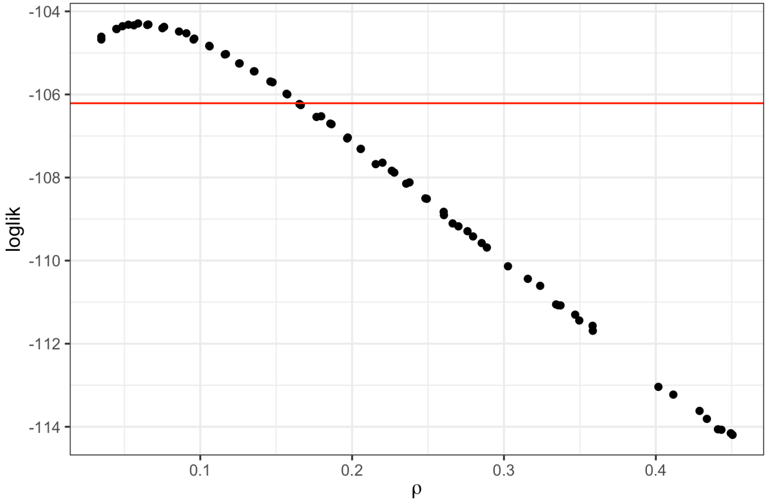
Profile: for the later parameters III

```r
foreach(guess=iter(guesses,"row"), .combine=rbind,
  .options.future=list(seed=2105684752)
) %dofuture% {
  mf1 |>
    mif2(params=guess,
      rw.sd=rw_sd(Beta=0.02,Eta=ivp(0.02))) |>
    mif2(Nmif=100,cooling.fraction.50=0.3) |>
    mif2() -> mf
  replicate(
    10,
    mf |> pfilter(Np=5000) |> logLik()) |>
    logmeanexp(se=TRUE) -> ll
  mf |> coef() |> bind_rows() |>
    bind_cols(loglik=ll[1],loglik.se=ll[2])
} -> results
```

Profile visualization: for the later parameters I



Profile visualization: for the later parameters II



Profile visualization: for the later parameters III

```r
results |>
  filter(loglik>max(loglik)-0.5*qchisq(df=1,p=0.95)) |>
  summarize(min=min(Rho),max=max(Rho)) -> rho_ci
```

Then we know reporting efficiencies ρ is in the 3.4–16% range (95% CI).

Prediction I

After all these analyses, we would like to visualize how exactly the model with the MLEs matches the data. We can do it by plotting the simulations with 95% the prediction interval.

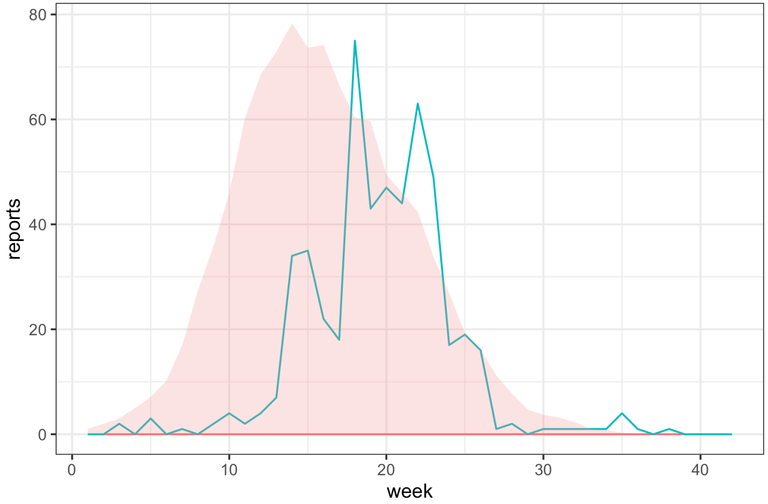
```r
read_csv("measles_params.csv") |>
  filter(loglik == max(loglik)) |>
  select(-loglik, -loglik.se) -> best.params

measSIR |>
  simulate(
    params=unlist(best.params),
    nsim=1000, format="data.frame", include.data=TRUE
  ) -> sims
```

Prediction II

```r
sims |>
  mutate(data=.id=="data") |>
  group_by(week,data) |>
  reframe(
    p=c(0.025,0.5,0.975),
    value=wquant(reports,probs=p),
    name=c("lo","med","up")
  ) |>
  select(-p) |> pivot_wider() |> ungroup() |>
  ggplot(aes(x=week,y=med,color=data,fill=data,ymin=lo,ymax=up))+
  geom_line()+ geom_ribbon(alpha=0.2,color=NA) +
  labs(y="reports")+
  theme_bw() + guides(color="none",fill="none")
```

Prediction III



License, acknowledgments, and links

- This lesson is prepared for the Simulation-based Inference for Epidemiological Dynamics module at the Summer Institute in Statistics and Modeling in Infectious Diseases, SISMID.
- The materials build on previous versions of this course and related courses.

- Produced with R version 4.4.0 and pomp version 5.9.
- Compiled on 2024-07-24.

Back to Lesson
R code for this lesson