

POMP group-level results - All boxes

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2023-06-22

Load required packages

```
library(tidyverse)

## -- Attaching packages ----- tidyverse 1.3.2 --
## v ggplot2 3.4.1     v purrr   1.0.1
## v tibble  3.1.8     v dplyr   1.1.0
## v tidyr   1.3.0     v stringr 1.5.0
## v readr   2.1.4     v forcats 1.0.0
## -- Conflicts ----- tidyverse_conflicts() --
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()   masks stats::lag()
```

```
library(stringi)
library(doParallel)
```

```
## Loading required package: foreach
##
## Attaching package: 'foreach'
##
## The following objects are masked from 'package:purrr':
##
##       accumulate, when
##
## Loading required package: iterators
## Loading required package: parallel
```

```
library(pomp)
```

```
##
## Welcome to pomp!
##
## As of version 4.6, no user-visible pomp function has a name that
## includes a dot ('.'). Function names have been changed to replace the
## dot with an underscore ('_'). For more information, see the pomp blog:
## https://kingaa.github.io/pomp/blog.html.
##
```

```

## Attaching package: 'pomp'
##
## The following object is masked from 'package:purrr':
##
##     map

library(panelPomp)
library(ggpubr)

```

Set working directory

```
setwd("~/Documents/GitHub/bdd/nw11_hier/final_files/")
```

Colour-blind friendly colour palette

```
cbPalette <- c("#999999", "#E69F00", "#56B4E9", "#009E73", "#F0E442", "#0072B2", "#D55E00", "#CC79A7")
```

Read in PNAS data

```

## # A tibble: 6 x 11
##   day      Pd      RBC    Ter119    CD71 mouseid paba   box   mouse Eryth  Retic
##   <int>    <dbl>    <dbl>    <dbl>    <dbl> <chr>   <dbl> <chr> <dbl> <dbl>
## 1     0       NA 8360000 5105135. 1.37e5 01-01   0.05  01    01   8.14e6 2.25e5
## 2     1      7934. 8290000 2745516. 1.94e5 01-01   0.05  01    01   7.70e6 5.86e5
## 3     2     19489. 7560000 2551937. 1.51e5 01-01   0.05  01    01   7.11e6 4.46e5
## 4     3    228842. 7820000 6400210. 4.98e5 01-01   0.05  01    01   7.21e6 6.08e5
## 5     4   1534425  7520000 3471975. 4.16e5 01-01   0.05  01    01   6.62e6 9.01e5
## 6     5  4528560  7600000 4748225. 5.50e5 01-01   0.05  01    01   6.72e6 8.80e5

```

Obtain estimates for beta and dose

```

##   box mouse mouseid      Beta      dose sigmaPd sigmaRBC sigmaRetic sigmaW
## 1  01   01   01-01 6.511778 793.298642      2     0.1      0.3      1
## 2  01   02   01-02 6.511778  3.444740      2     0.1      0.3      1
## 3  01   03   01-03 6.511778 420.158396      2     0.1      0.3      1
## 4  02   01   02-01 6.090502 607.635623      2     0.1      0.3      1
## 5  02   02   02-02 6.090502 260.448444      2     0.1      0.3      1
## 6  02   03   02-03 6.090502  1.348118      2     0.1      0.3      1
##   sigmaN sigmaR   E_0   R_0   W_0   N_0
## 1     0.5     0.5 8e+06 3e+05 88000 8e+05
## 2     0.5     0.5 8e+06 3e+05 88000 8e+05
## 3     0.5     0.5 8e+06 3e+05 88000 8e+05
## 4     0.5     0.5 8e+06 3e+05 88000 8e+05
## 5     0.5     0.5 8e+06 3e+05 88000 8e+05
## 6     0.5     0.5 8e+06 3e+05 88000 8e+05

```

Create object pos with pomp object for each mouse

```

foreach (m = iter(theta,"row"), .inorder=TRUE,.combine=c) %dopar% {

  flow %>%
    filter(mouseid==m$mouseid) %>%
    select(day,Pd,RBC,Retic) %>%
    mutate(Retic=if_else(day %in% c(0,14),NA_real_,Retic)) %>%
    pomp(
      params=select(m,-mouseid,-box,-mouse) %>% unlist(),
      times="day",
      t0=0,
      rmeasure=Csnippet("
        Retic = rlnorm(log(1+R),sigmaRetic)-1;
        RBC = rlnorm(log(1+E+R),sigmaRBC)-1;
        Pd = rlnorm(log(1+K),sigmaPd)-1;");
      dmeasure=Csnippet("
        double l1, l2, l3;
        l1 = (R_FINITE(Retic)) ? dlnorm(1+Retic,log(1+R),sigmaRetic,1) : 0;
        l2 = (R_FINITE(RBC)) ? dlnorm(1+RBC,log(1+E+R),sigmaRBC,1) : 0;
        l3 = (R_FINITE(Pd) && Pd>0) ? dlnorm(1+Pd,log(1+K),sigmaPd,1) : 0;
        lik = (give_log) ? l1+l2+l3 : exp(l1+l2+l3);"),
      rprocess=discrete_time(
        step.fun=Csnippet("
          double Mold = M;
          M = Beta*K*exp(-(W+N)/(R+E));
          E = (R+E)*exp(-(Mold+N)/(R+E));
          N = rlnorm(log(N),sigmaN);
          W = rlnorm(log(W),sigmaW);
          R = rlnorm(log(R),sigmaR);
          K = (R+E>0) ? (R+E)*(1-exp(-M/(R+E))): 0;
        "),
        delta.t=1
      ),
      partrans=parameter_trans(
        log=c("sigmaW","sigmaR","sigmaN",
              "sigmaPd","sigmaRBC","sigmaRetic",
              "N_0","W_0","E_0","R_0")
      ),
      rinit=Csnippet("
        E = E_0;
        R = R_0;
        N = N_0;
        W = W_0;
        M = 0;
        K = dose;"),
      statenames=c("E","R","W","N","M","K"),
      paramnames=c(
        "Beta","dose",
        "sigmaPd","sigmaRBC","sigmaRetic",
        "sigmaW","sigmaN","sigmaR",
        "E_0","R_0","W_0","N_0"
      )
    )
}

```

```

        )
} %>%
  set_names(theta$mouseid) -> pos

```

Obtain MLE for sigmas, initial values, betas and dose

```

##      loglik    sigmaW    sigmaN    sigmaPd    sigmaR    sigmaRBC sigmaRetic      E_0
## 1 -11217.79 1.043139 0.624558 0.5966612 0.392552 0.07942614 0.1514119 7722711
##          N_0        R_0        W_0
## 1 410608.7 617657.5 176481.2

## # A tibble: 15 x 3
##   mouseid     Beta     dose
##   <chr>     <dbl>   <dbl>
## 1 01-01     6.51   793.
## 2 01-02     6.51    3.44
## 3 01-03     6.51   420.
## 4 02-01     6.09   608.
## 5 02-02     6.09   260.
## 6 02-03     6.09    1.35
## 7 03-01     5.76   591.
## 8 03-02     5.76   382.
## 9 03-03     5.76   317.
## 10 04-01    4.08  1476.
## 11 04-02    4.08   716.
## 12 04-03    4.08  1139.
## 13 05-01     0       0
## 14 05-02     0       0
## 15 05-03     0       0

```

Load in PNAS trajectories

```

sm1name <- "m5sm1.rds"
sm1 <- readRDS(sm1name)

```

Create dataframe with weighted trajectories (grouped by mouseid first, then by box)

```

sm1 |>
  as_tibble() |>
  filter(mouseid!="01-02",mouseid!="02-03") |> #remove underdosed mice
  pivot_wider(names_from=variable,values_from=value) |>
  left_join(bdf,by=c("mouseid")) |>
  separate_wider_delim(cols="mouseid",delim="-",names=c("box","mouse"),cols_remove=FALSE) |>
  group_by(mouseid) |>
  mutate(
    SM=exp(-M/(R+E)),
    SN=exp(-N/(R+E)),

```

```

SW=exp(-W/(R+E)),
Qps=(1-SM)*SW*SN,
Qpn=N/(N+W)*(1-SM)*(1-SW*SN),
Qpw=W/(N+W)*(1-SM)*(1-SW*SN),
Qun=SM*(1-SN),
Qus=SM*SN,
lambda_r=Beta*R/M*Qps,
lambda_e=Beta*E/M*Qps,
lambda_n=Beta*(R+E)/M*Qpn,
lambda_w=Beta*(R+E)/M*Qpw,
lambda_u=Beta-lambda_r-lambda_e-lambda_n-lambda_w,
lambda_u_w_ratio=lambda_u/lambda_w,
lambda_u_n_ratio=lambda_u/lambda_n,
lambda_u_wn_ratio=lambda_u/(lambda_w+lambda_n),
loss=(R+E)*(1-Qus),
rbc=E+R,
varN=N/rbc,
perRetic=R/rbc,
lik=exp(loglik-max(loglik))
) |>
ungroup() |>
select(-loglik,-Beta,-dose) |>
gather(variable,value,-rep,-time,-mouse,-box,-lik,-mouseid) |>
filter(is.finite(value)) %>%
group_by(box,time,variable) |>
dplyr::reframe(
  value=pomp::wquant(x=value,probs=c(0.05,0.5,0.95),weights=lik),
  name=c("lo","med","hi")
) |>
ungroup() |>
pivot_wider() -> group_traj

group_traj$pABA <- factor(group_traj$box,levels=c("05","04","03","02","01"),
                           labels=c("Control","0%","0.05%","0.5%","5%"))

```

Remove estimates for W for control mice

```

group_traj <- group_traj |> dplyr::slice(-which(group_traj$box=="05"&group_traj$variable=="W"))

group_traj |>
  filter(time<=20,variable%in%c("rbc","E","R","N","W","K")) |>
  mutate(variable=case_match(variable,
                            "K"~"Parasites",
                            "rbc"~"RBC",
                            "R"~"Reticulocytes",
                            "E"~"Erythrocytes",
                            "N"~"Indiscriminate killing",
                            "W"~"Targeted killing")) |>

ggplot()+
  geom_line(aes(x=time,y=med,col=pABA))+ 
  geom_ribbon(aes(x=time,ymin=lo,ymax=hi,fill=pABA),alpha=0.2)+
```

```

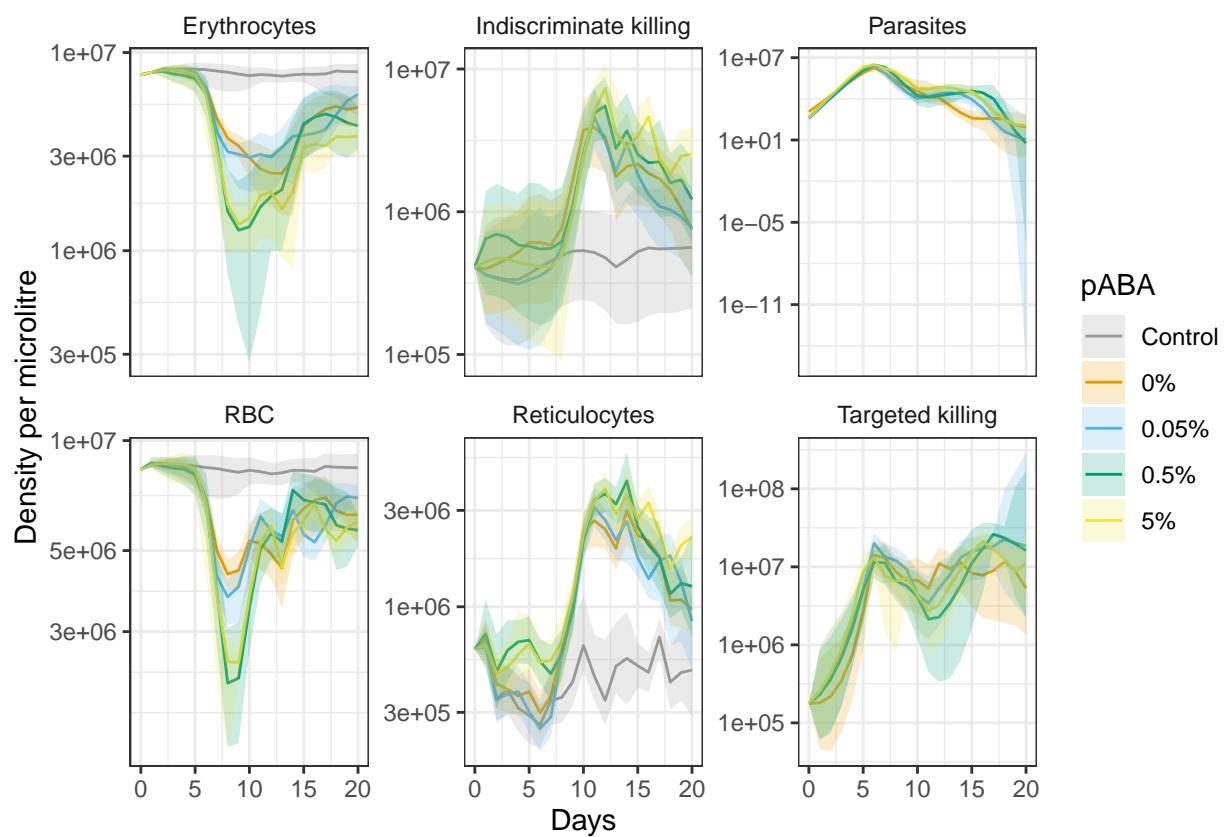
scale_y_log10()+
scale_colour_manual(values=cbPalette)+
scale_fill_manual(values=cbPalette)+
xlab("Days")+ylab("Density per microlitre")+
facet_wrap(variable~.,scales="free_y")+
theme_bw()+
theme(
  strip.background = element_blank()
)

```

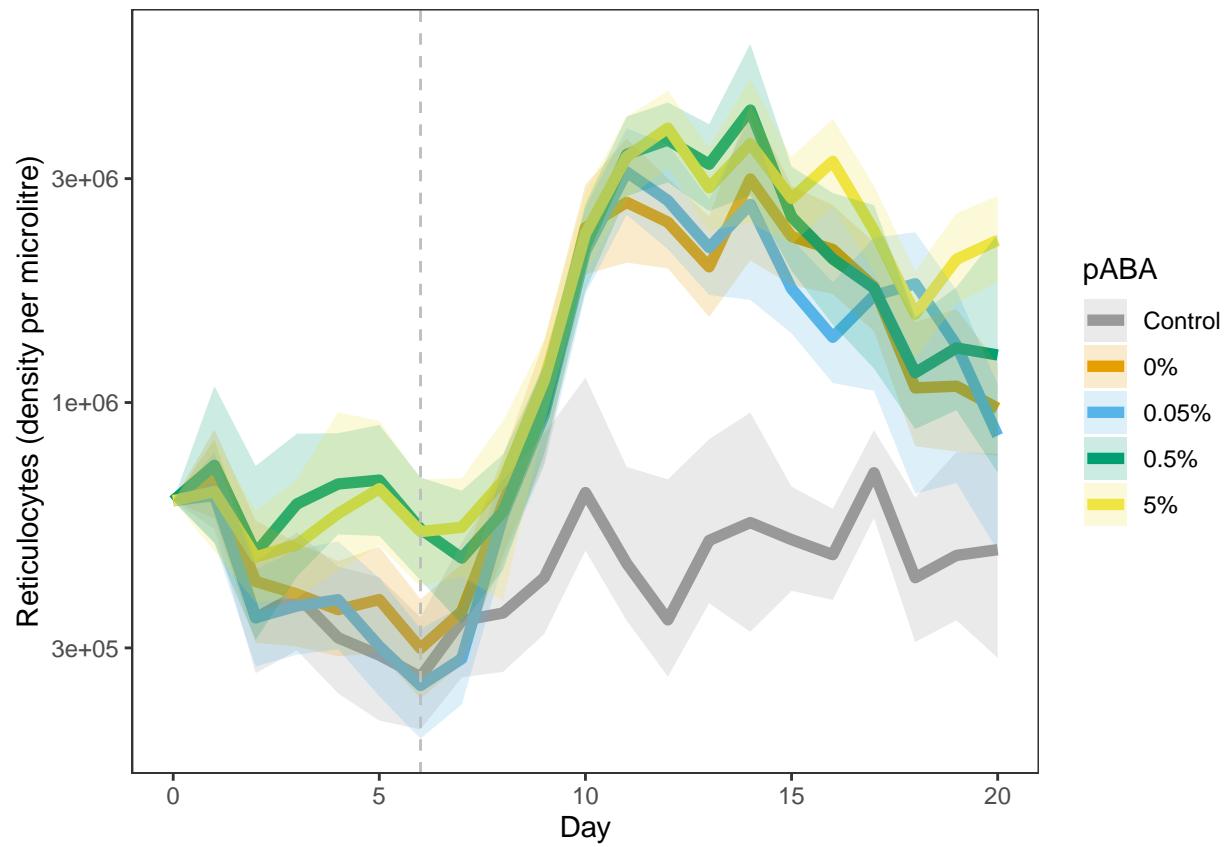
```

## Warning: Transformation introduced infinite values in continuous y-axis
## Transformation introduced infinite values in continuous y-axis
## Transformation introduced infinite values in continuous y-axis

```

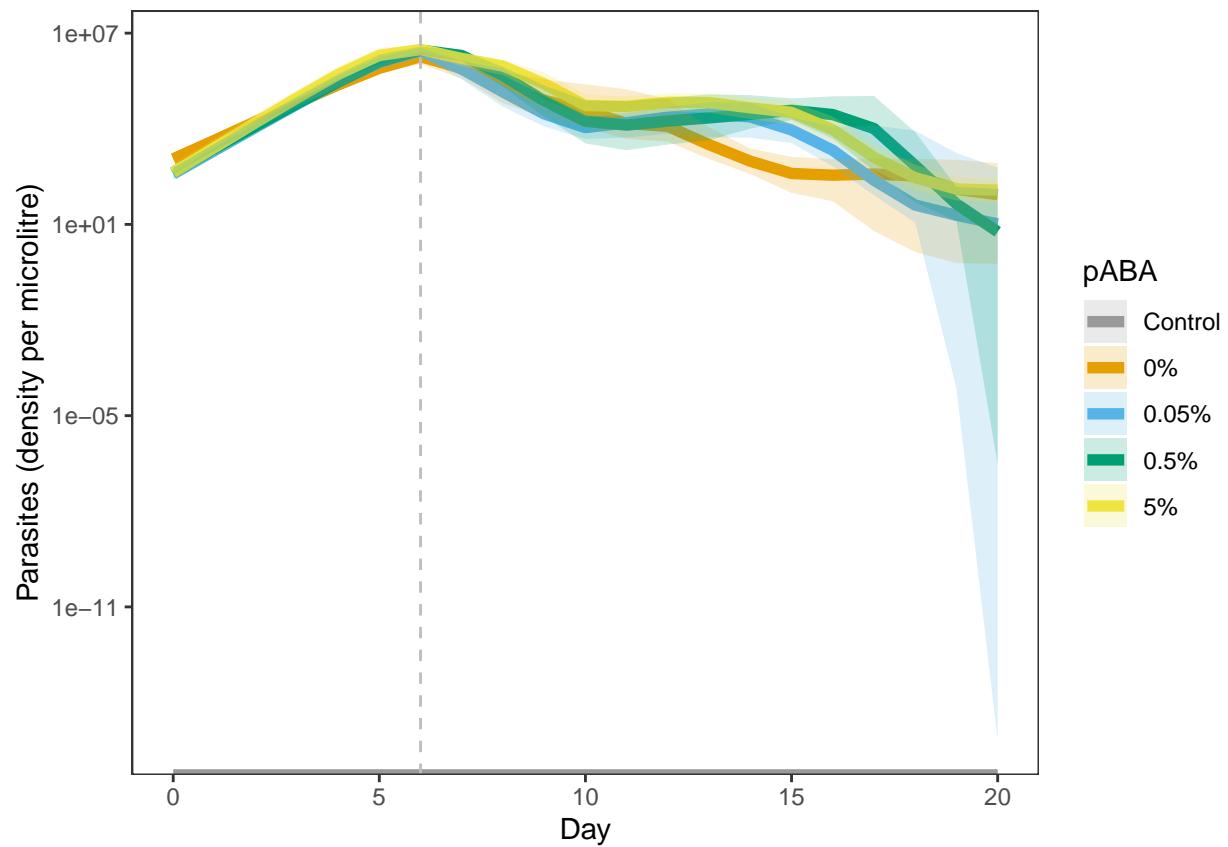


Plot group-level trajectories for reticulocytes with day of peak parasitaemia

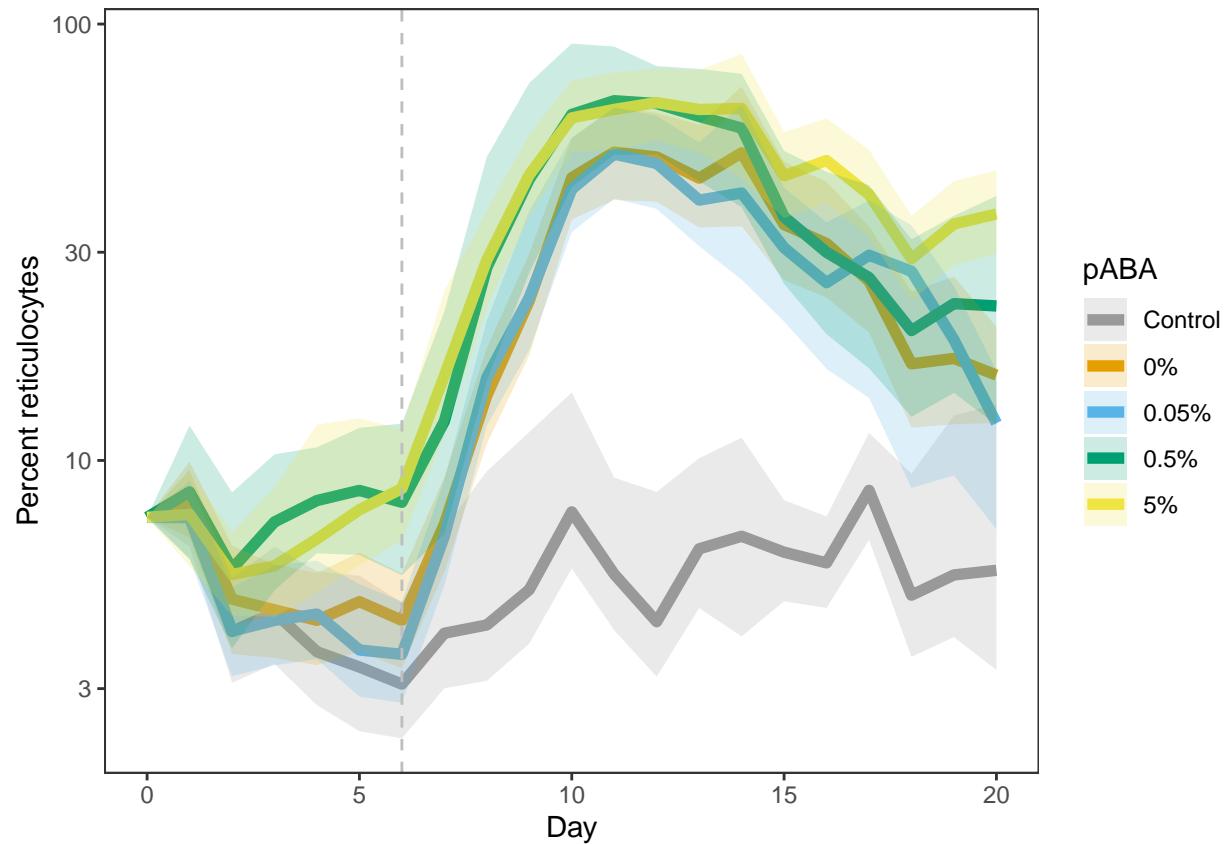


Plot group-level trajectories for parasite density

```
## Warning: Transformation introduced infinite values in continuous y-axis
## Transformation introduced infinite values in continuous y-axis
## Transformation introduced infinite values in continuous y-axis
```



Plot group-level trajectories for percent reticulocytes



Create swirly data frame

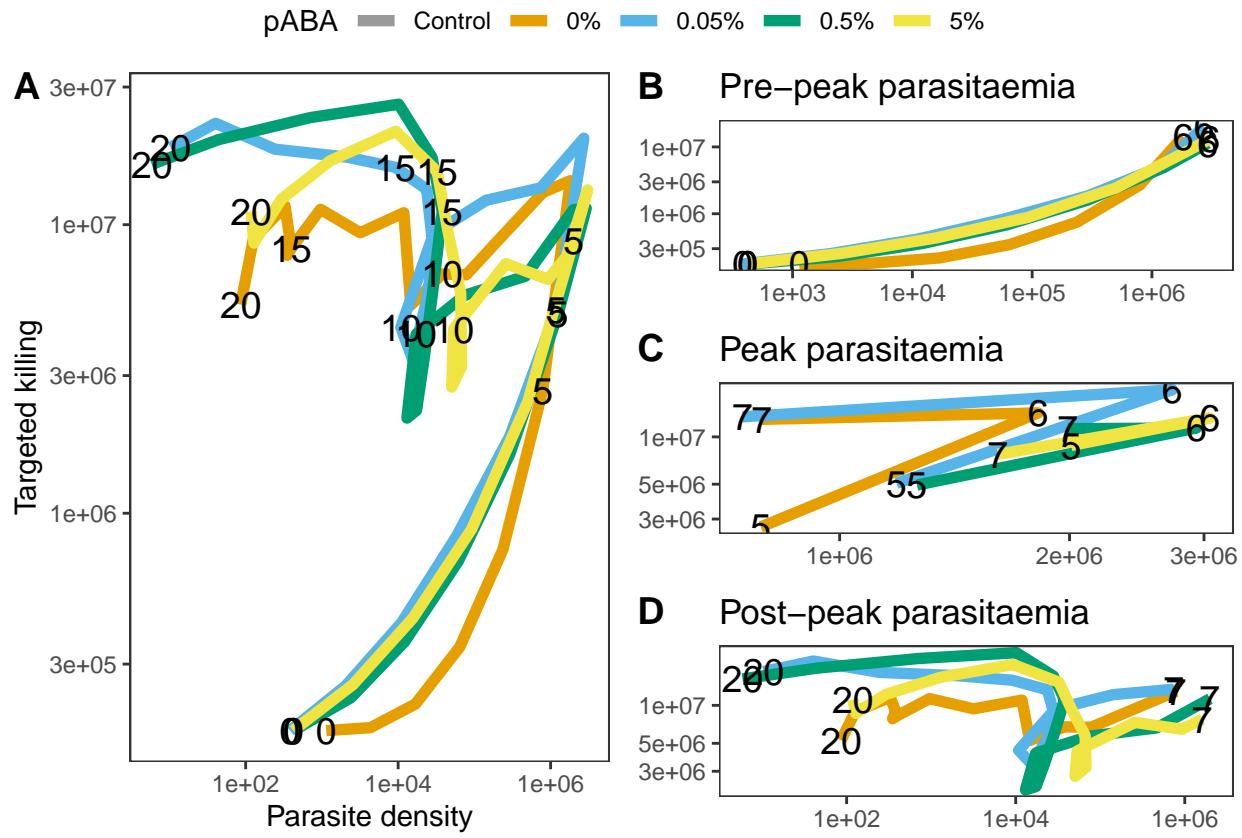
```
## # A tibble: 6 x 29
##   box    time pABA      E      K      M      N      Qpn      Qps      Qpw      Qun
##   <chr> <int> <fct>    <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>   <dbl>
## 1 01     0 5%  7722711. 4.20e2 0       4.11e5 0       0       0       0       0.0480
## 2 01     1 5%  7939703. 2.55e3 2.55e3 4.44e5 1.52e-5 2.78e-4 1.02e-5 0.0503
## 3 01     2 5%  8165549. 1.56e4 1.56e4 4.74e5 9.34e-5 1.63e-3 1.04e-4 0.0532
## 4 01     3 5%  8166517. 9.22e4 9.27e4 4.66e5 5.29e-4 9.04e-3 1.15e-3 0.0523
## 5 01     4 5%  8085821. 5.03e5 5.18e5 4.40e5 2.45e-3 4.01e-2 1.54e-2 0.0470
## 6 01     5 5%  7717184. 2.01e6 2.29e6 4.26e5 7.74e-3 7.99e-2 1.48e-1 0.0370
## # ... with 18 more variables: Qus <dbl>, R <dbl>, SM <dbl>, SN <dbl>, SW <dbl>,
## #   W <dbl>, loss <dbl>, perRetic <dbl>, rbc <dbl>, varN <dbl>, lambda_e <dbl>,
## #   lambda_n <dbl>, lambda_r <dbl>, lambda_u <dbl>, lambda_u_n_ratio <dbl>,
## #   lambda_u_w_ratio <dbl>, lambda_u_wn_ratio <dbl>, lambda_w <dbl>
```

Parasite density versus targeted killing

```
## Warning: Transformation introduced infinite values in continuous x-axis
## Transformation introduced infinite values in continuous x-axis

## Warning: Removed 7 rows containing missing values ('geom_path()').
```

```
## Warning: Removed 2 rows containing missing values ('geom_text()').  
  
## Warning: Transformation introduced infinite values in continuous x-axis  
## Transformation introduced infinite values in continuous x-axis  
  
## Warning: Removed 3 rows containing missing values ('geom_path()').  
  
## Warning: Removed 3 rows containing missing values ('geom_text()').  
  
## Warning: Transformation introduced infinite values in continuous x-axis  
## Transformation introduced infinite values in continuous x-axis  
  
## Warning: Removed 14 rows containing missing values ('geom_path()').  
  
## Warning: Removed 2 rows containing missing values ('geom_text()').  
  
## Warning: Transformation introduced infinite values in continuous x-axis  
## Transformation introduced infinite values in continuous x-axis  
  
## Warning: Removed 21 rows containing missing values ('geom_path()').  
  
## Warning: Removed 5 rows containing missing values ('geom_text()').  
  
## Warning: Transformation introduced infinite values in continuous x-axis  
## Transformation introduced infinite values in continuous x-axis  
  
## Warning: Removed 21 rows containing missing values ('geom_path()').  
  
## Warning: Removed 5 rows containing missing values ('geom_text()').
```



```

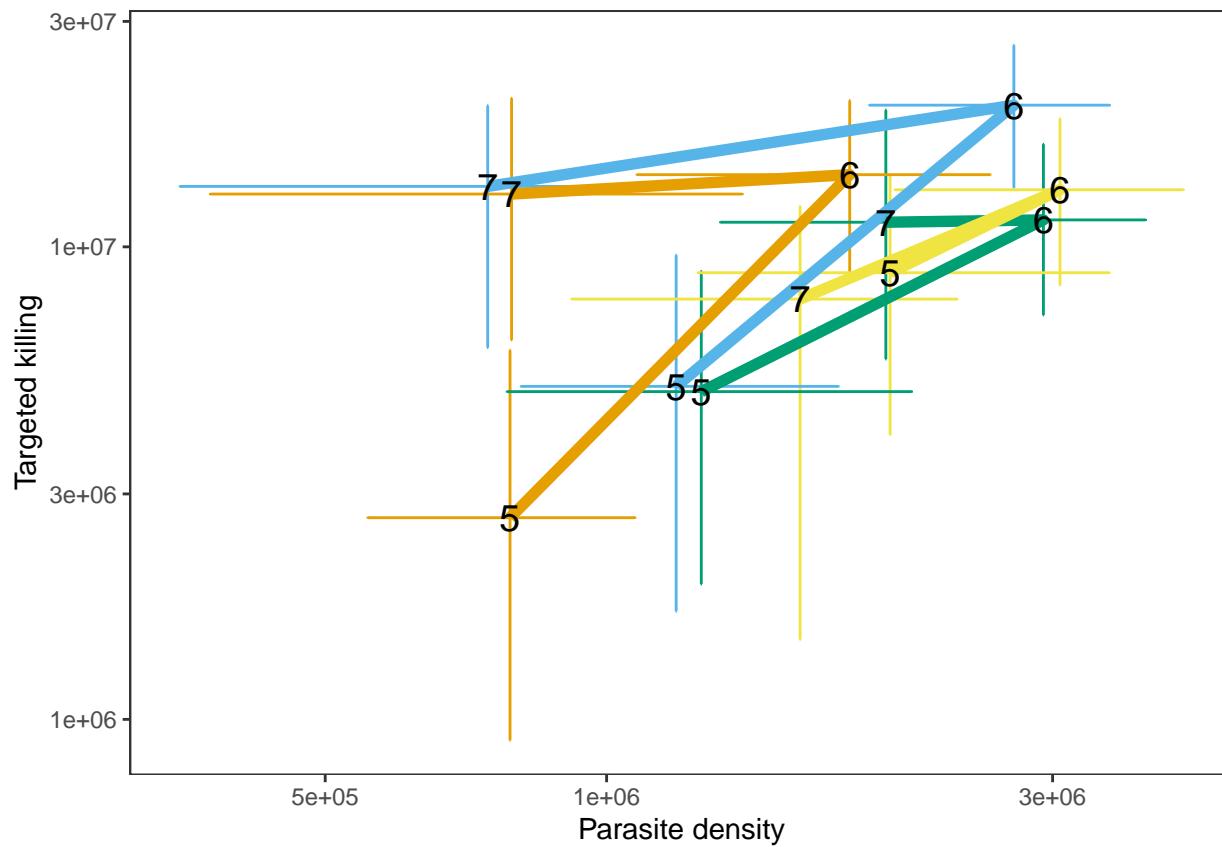
## Warning: Transformation introduced infinite values in continuous x-axis
## Transformation introduced infinite values in continuous x-axis

## Warning: Removed 3 rows containing missing values ('geom_errorbarh()').

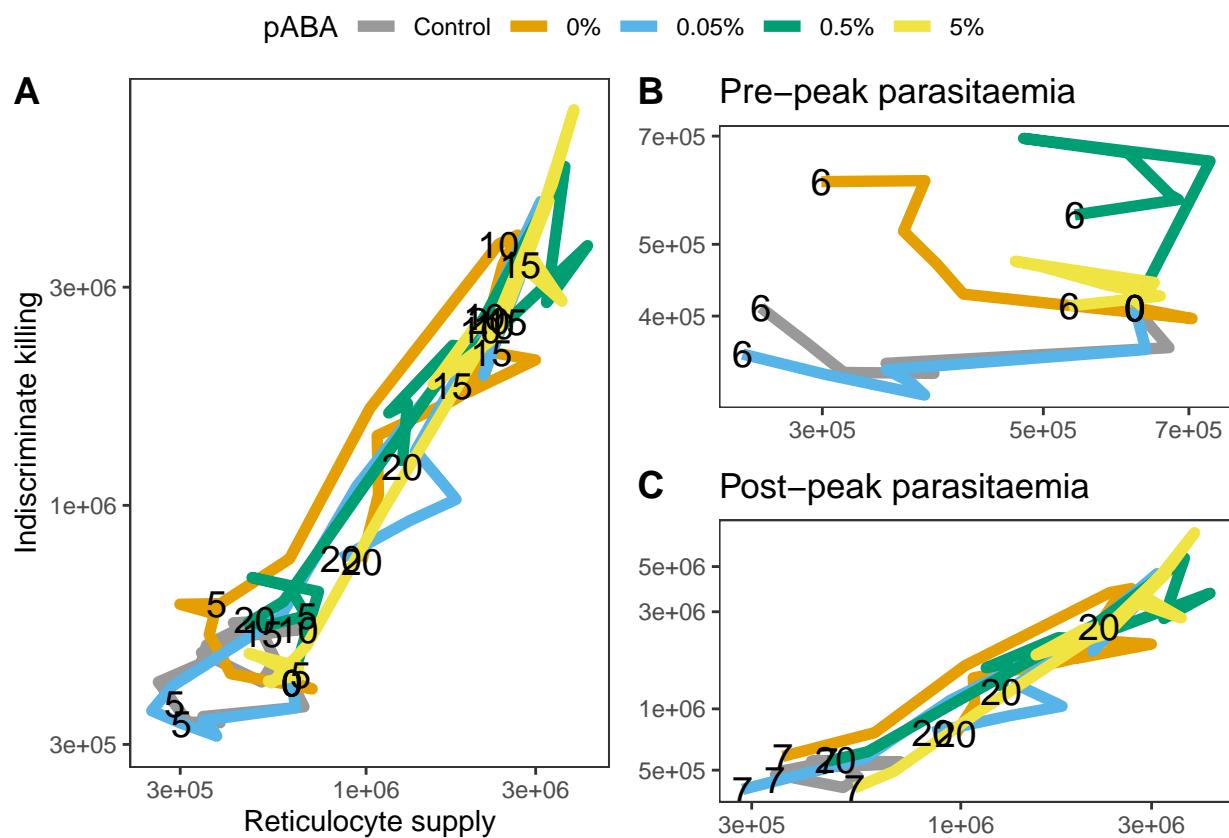
## Warning: Removed 3 rows containing missing values ('geom_path()').

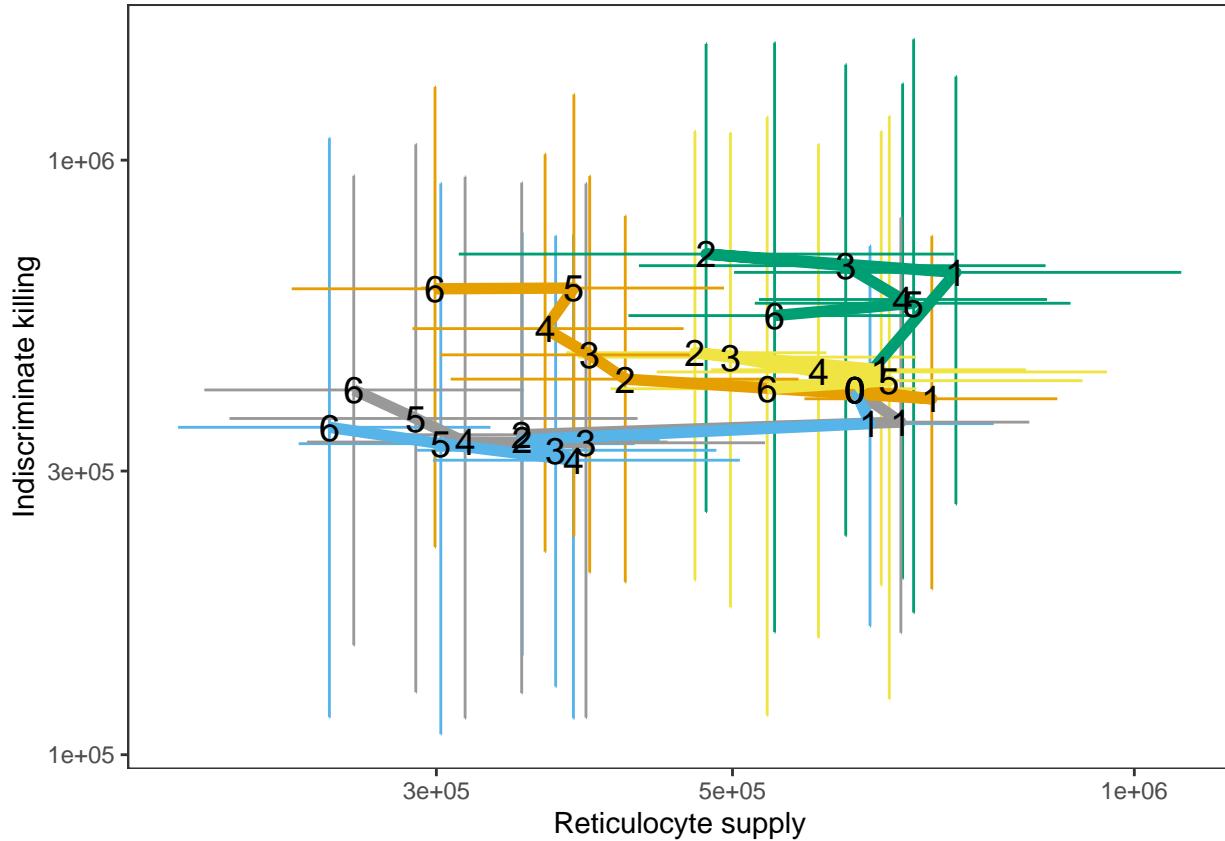
## Warning: Removed 3 rows containing missing values ('geom_text()').

```



Indiscriminate killing versus reticulocyte supply



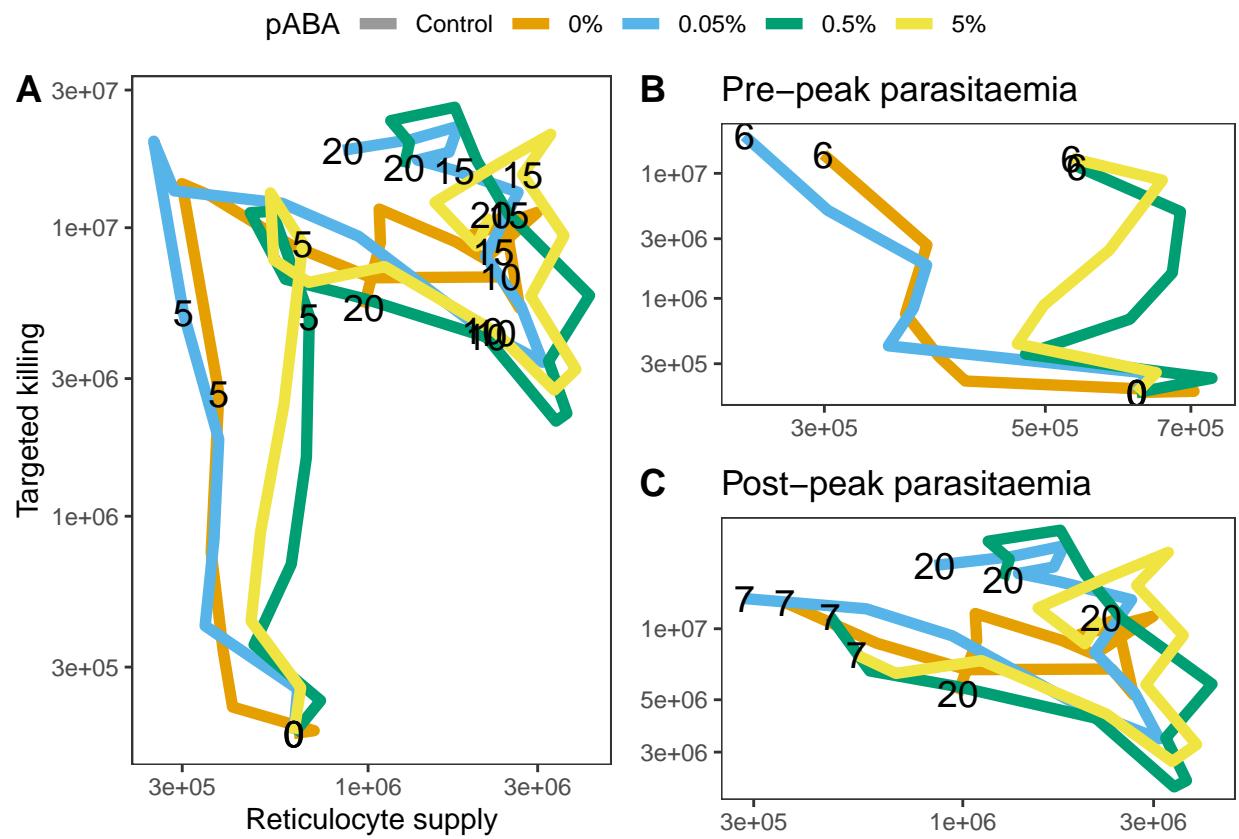


Targeted killing versus reticulocyte supply

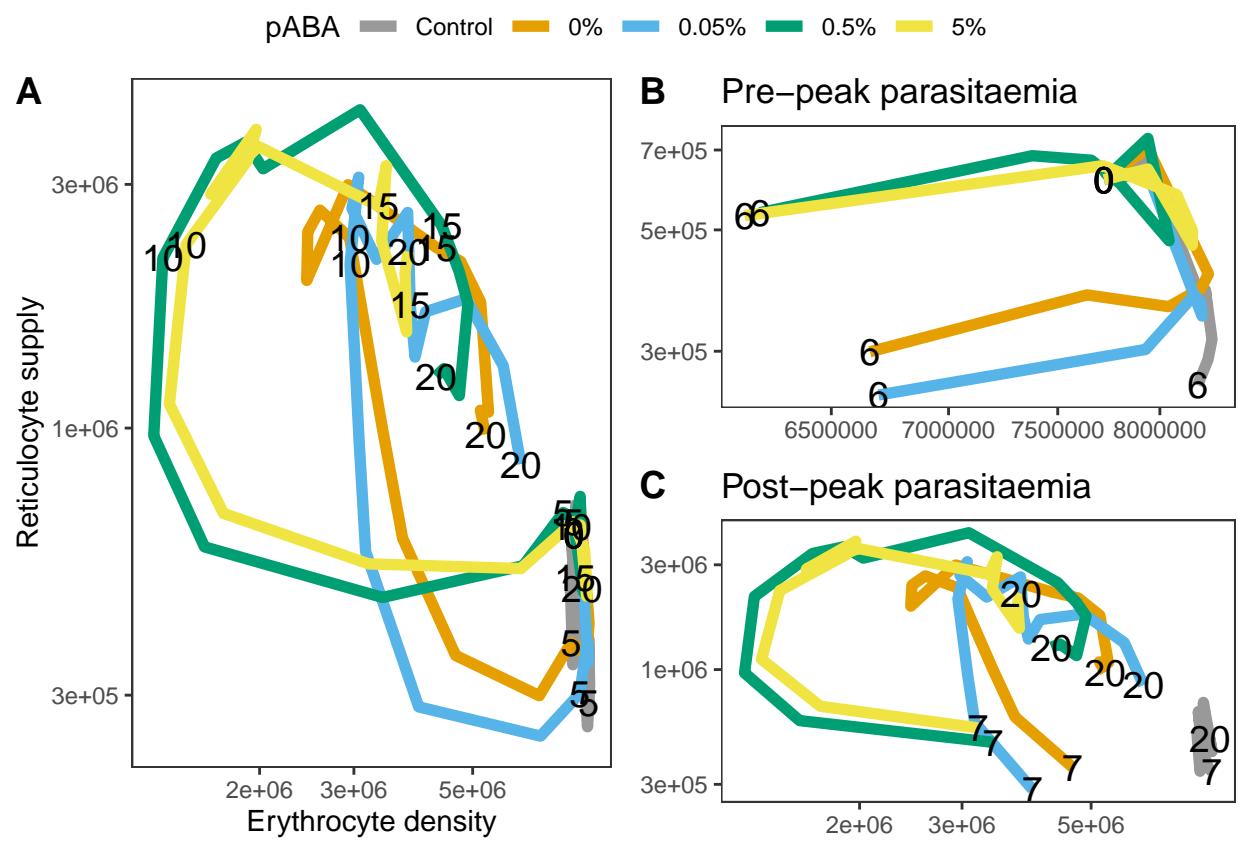
```

## Warning: Removed 7 rows containing missing values ('geom_path()').
## Warning: Removed 2 rows containing missing values ('geom_text()').
## Warning: Removed 14 rows containing missing values ('geom_path()').
## Warning: Removed 2 rows containing missing values ('geom_text()').
## Warning: Removed 21 rows containing missing values ('geom_path()').
## Warning: Removed 5 rows containing missing values ('geom_text()').
## Warning: Removed 21 rows containing missing values ('geom_path()').
## Warning: Removed 5 rows containing missing values ('geom_text()').

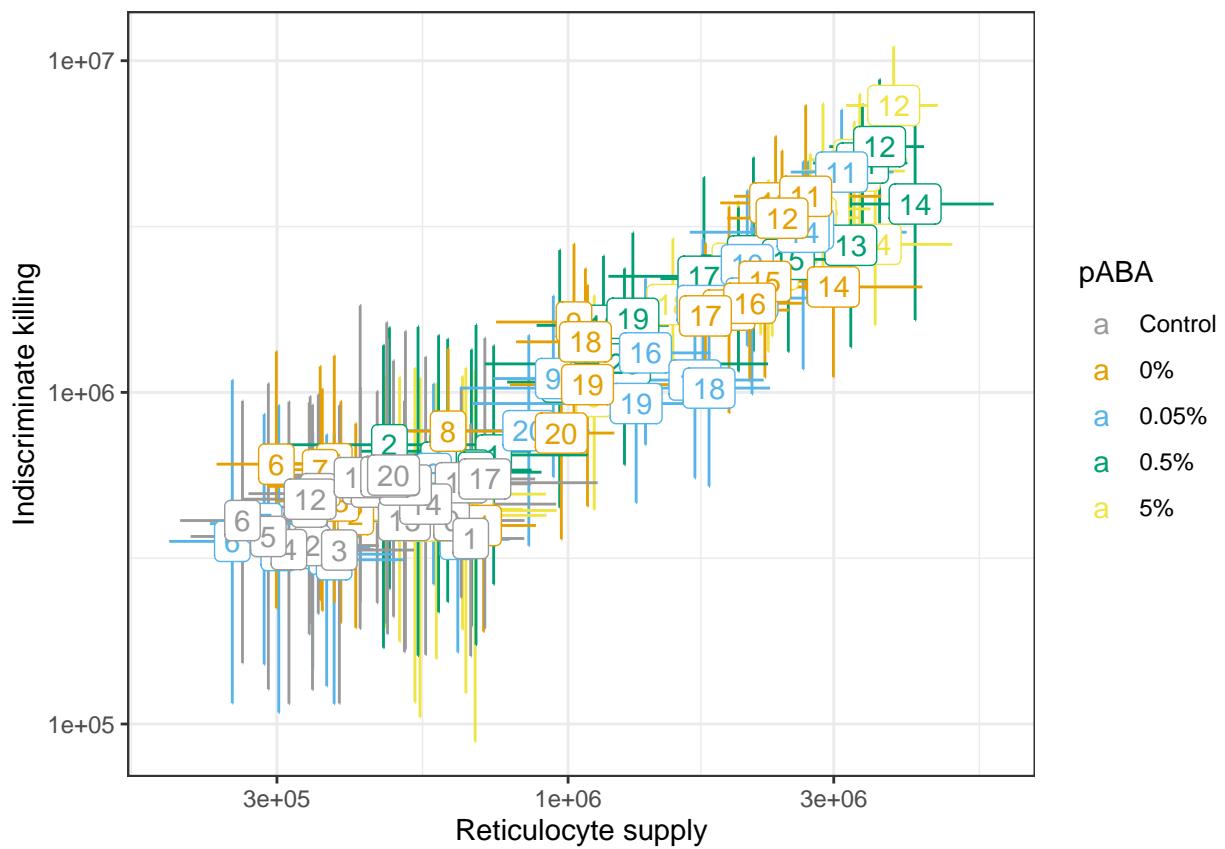
```

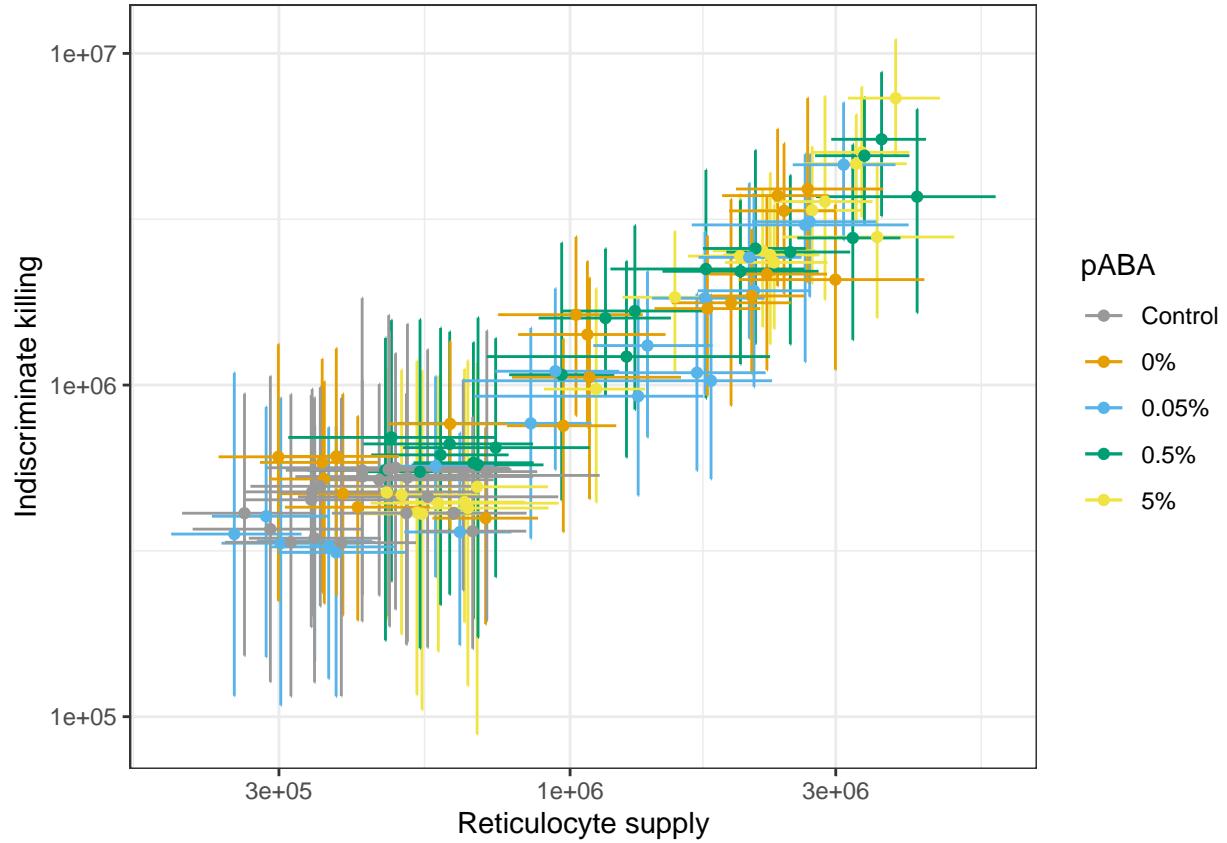


Reticulocyte supply versus erythrocyte density

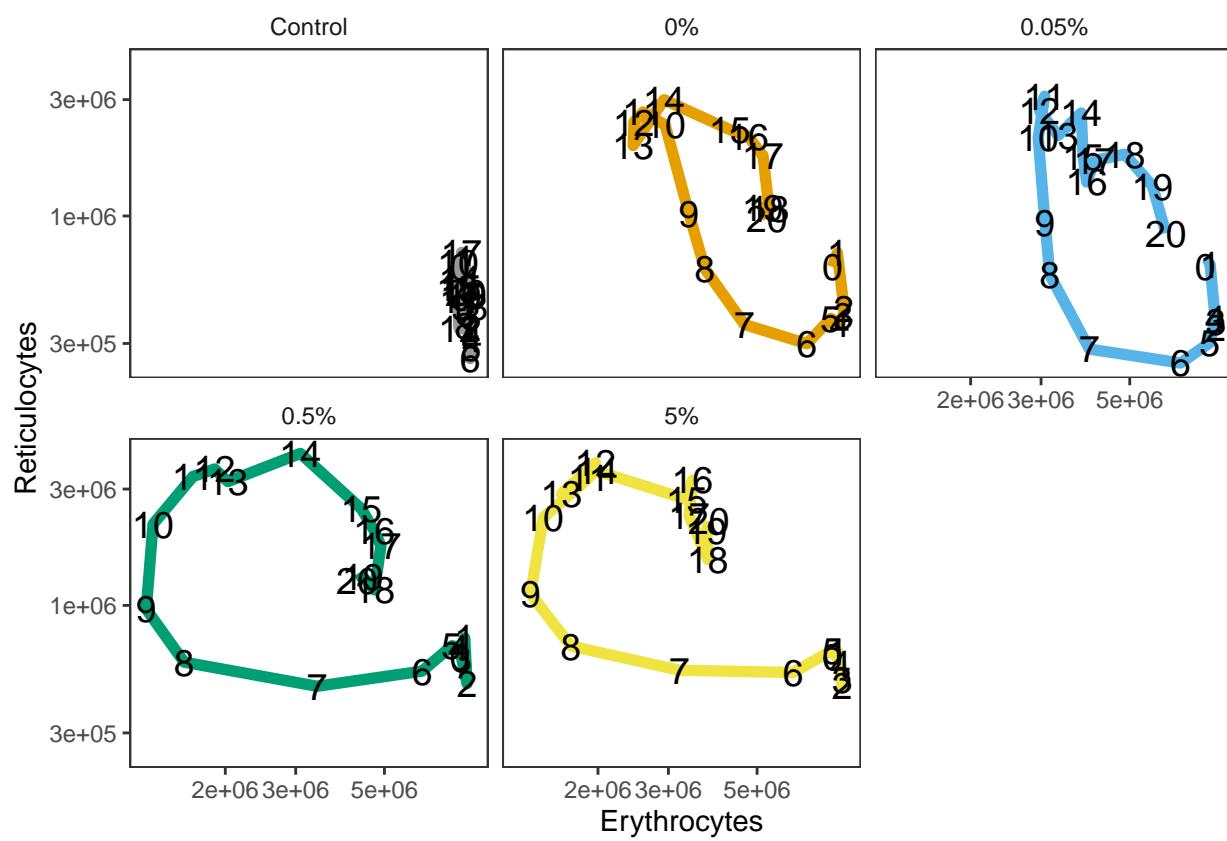


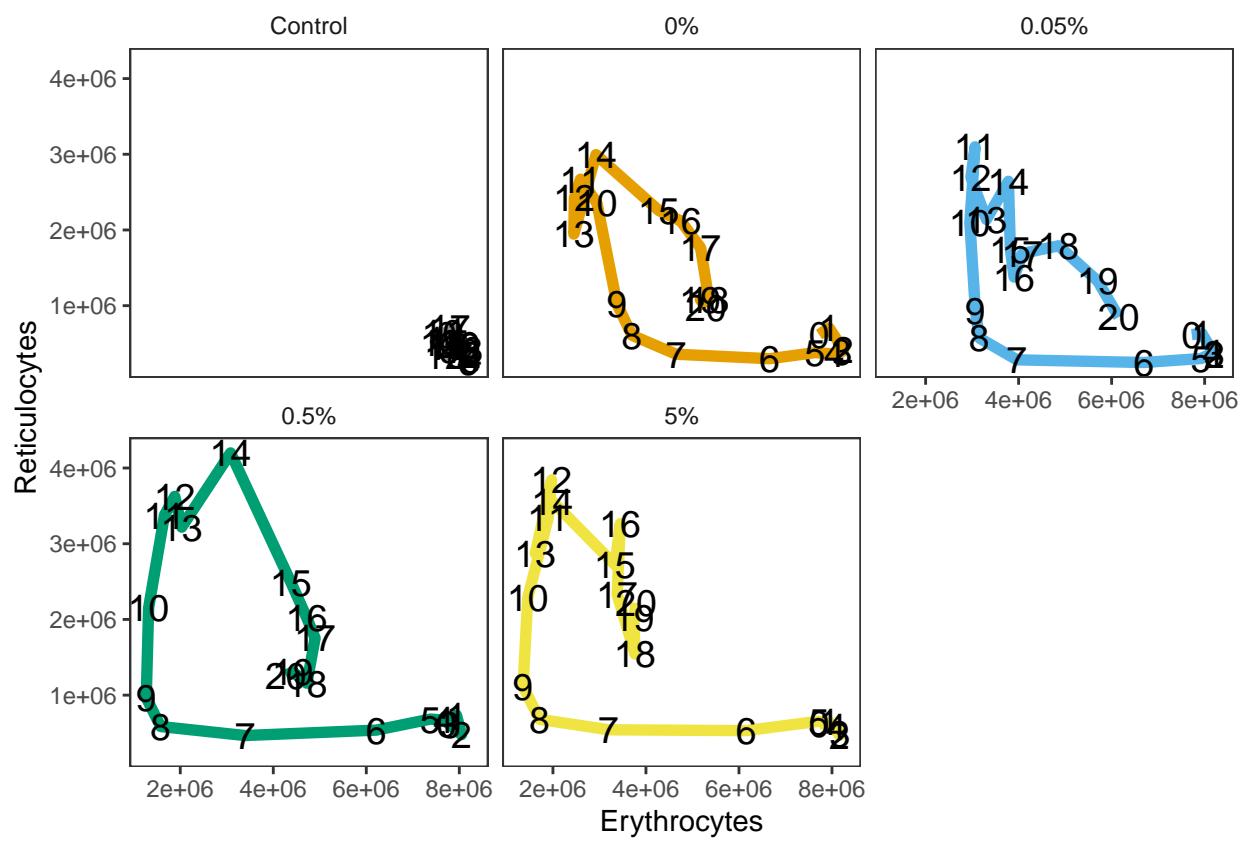
Plot N versus R with bi-directional error bars

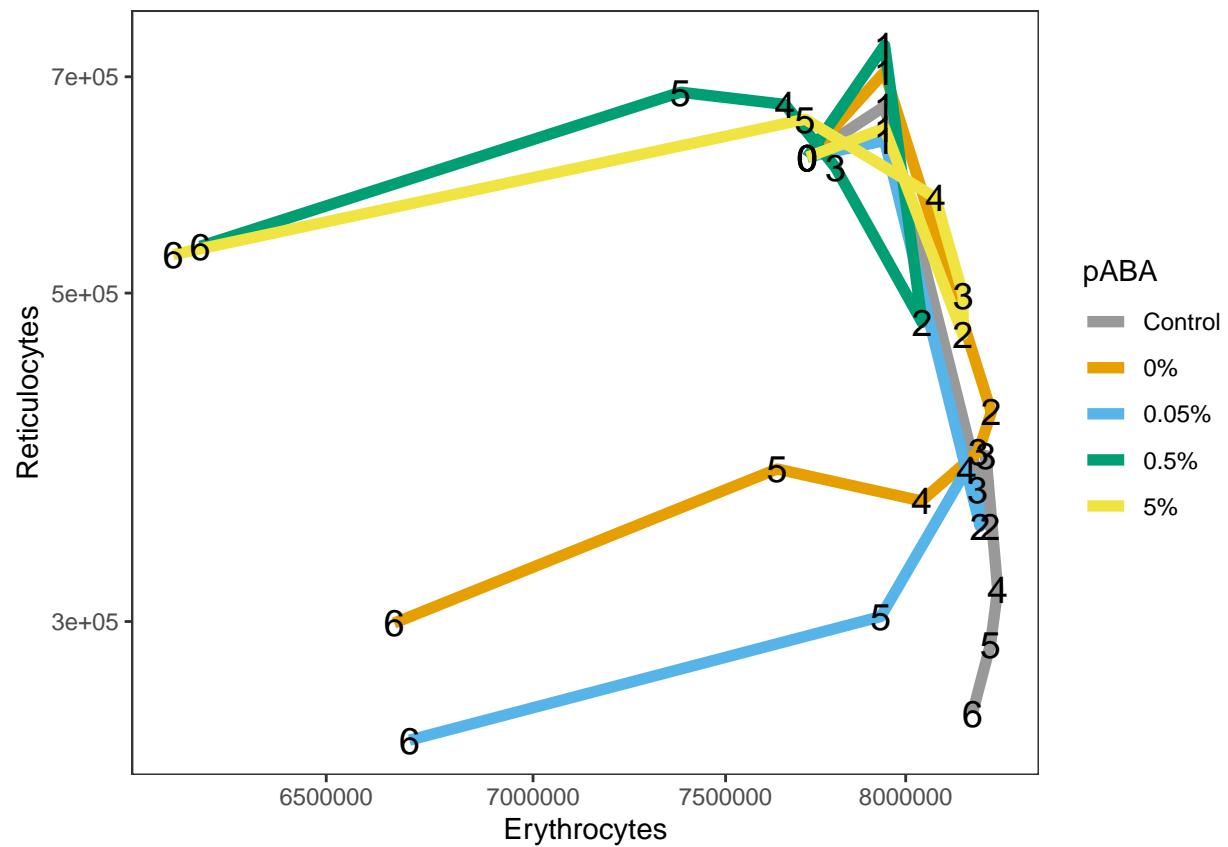


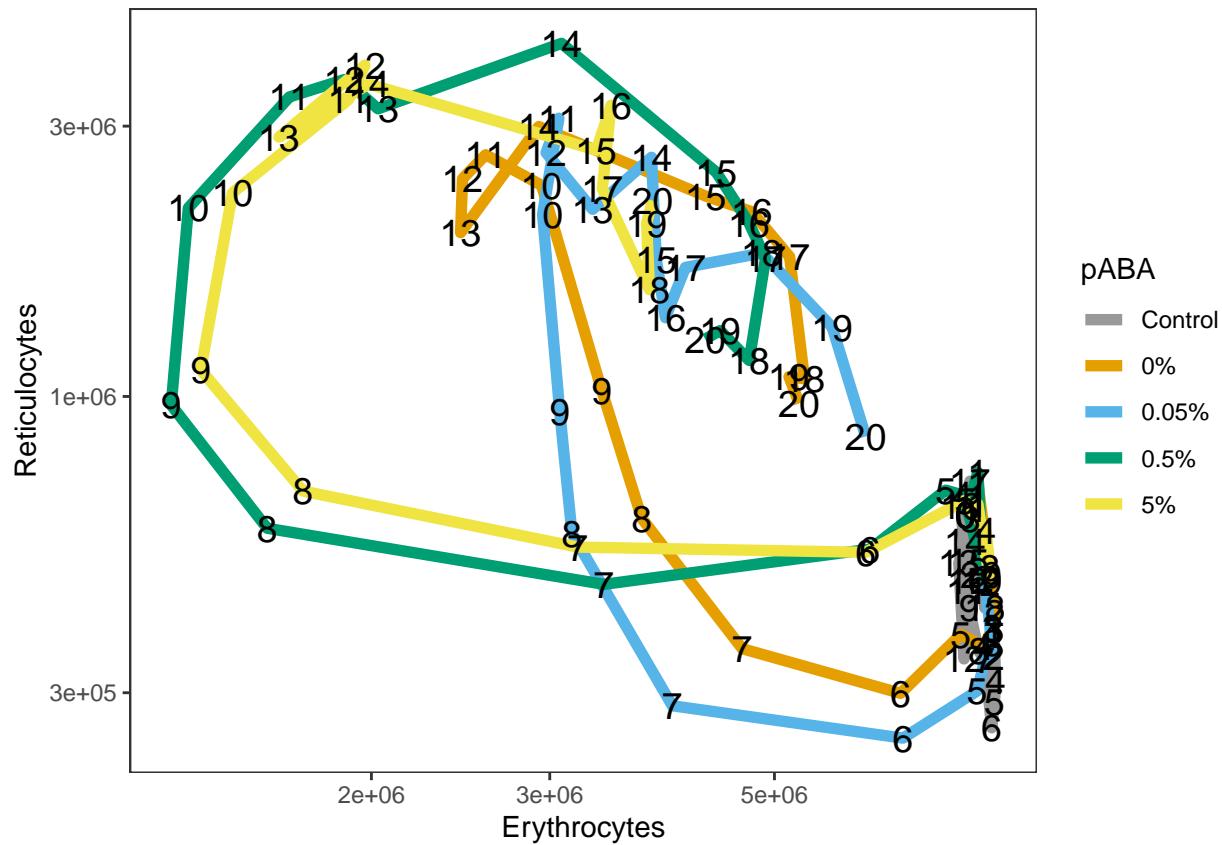


Plot reticulocytes versus erythrocytes





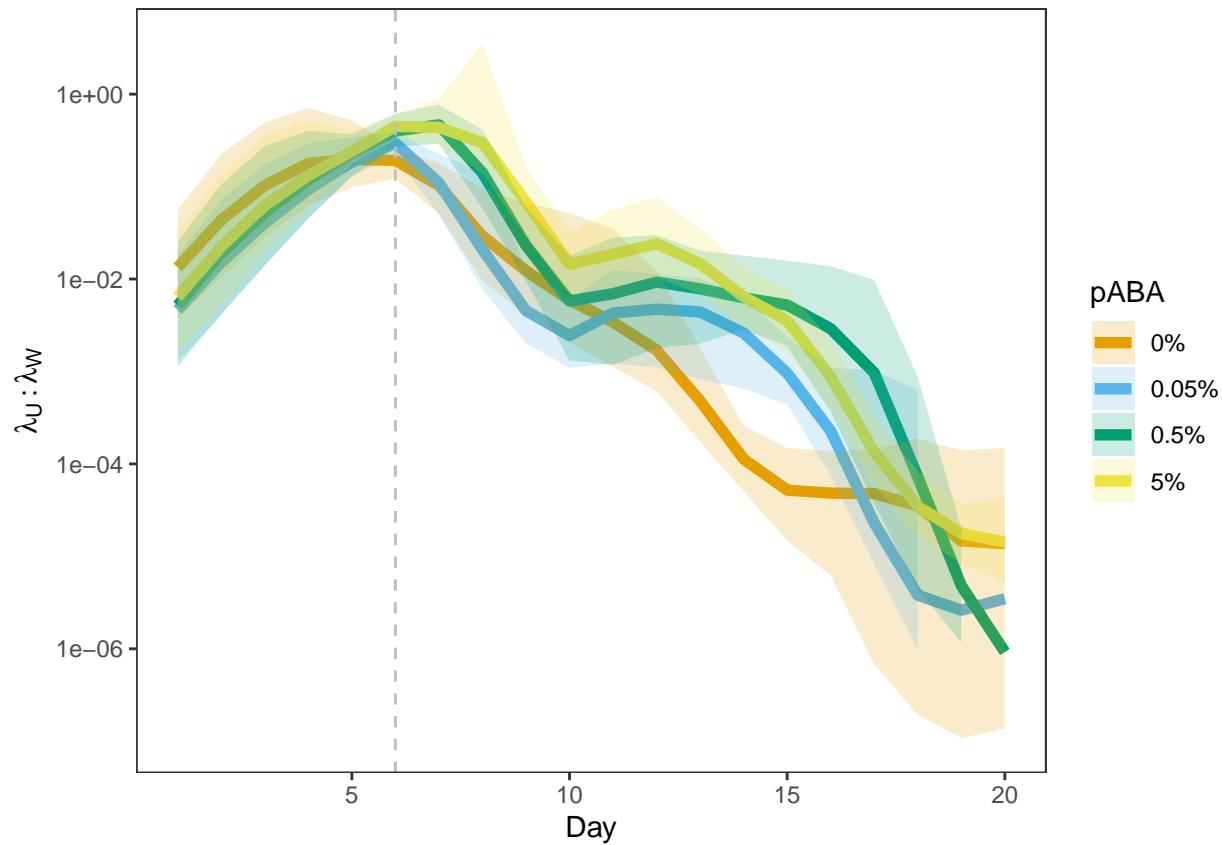




Ratio of λ_u to λ_w over time

```
## Warning in self$trans$transform(x): NaNs produced

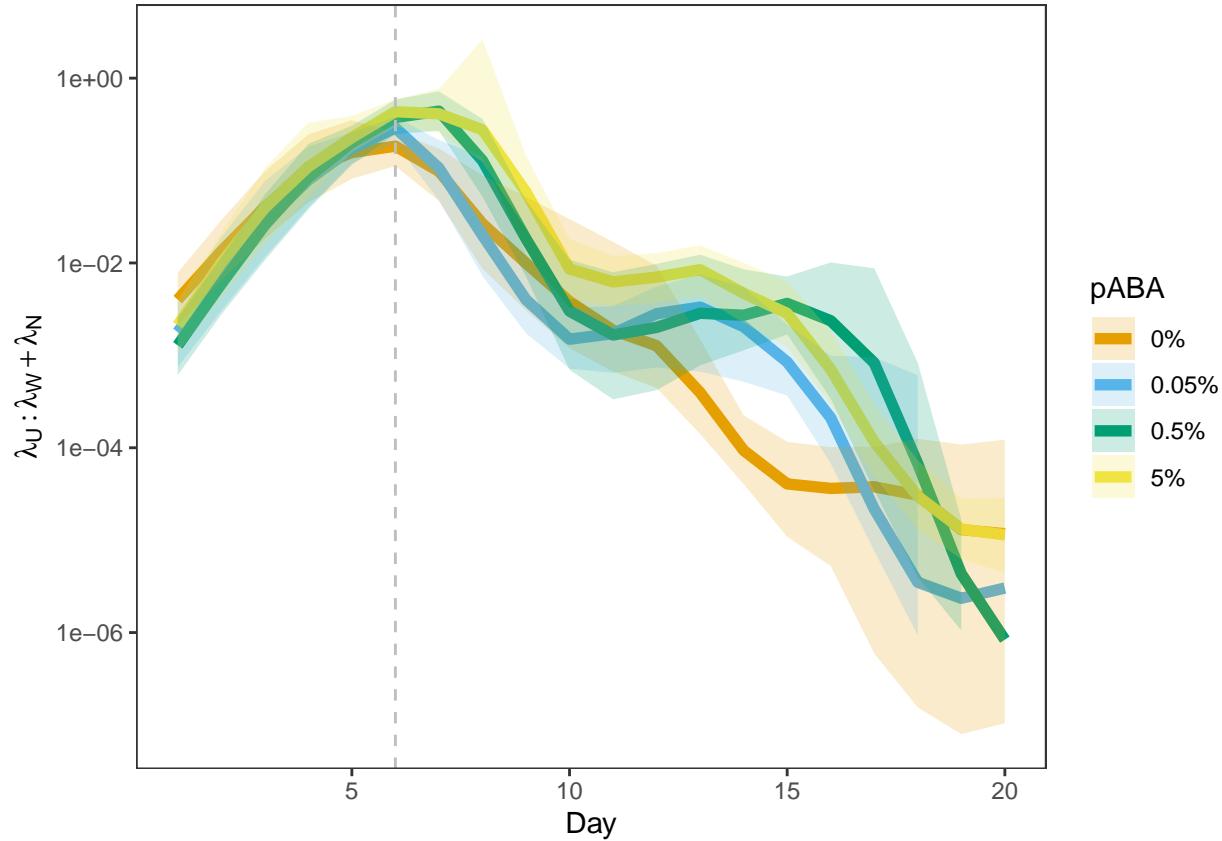
## Warning: Transformation introduced infinite values in continuous y-axis
```



Ratio of λ_u to $\lambda_w + \lambda_n$ over time

```
## Warning in self$trans$transform(x): NaNs produced

## Warning: Transformation introduced infinite values in continuous y-axis
```

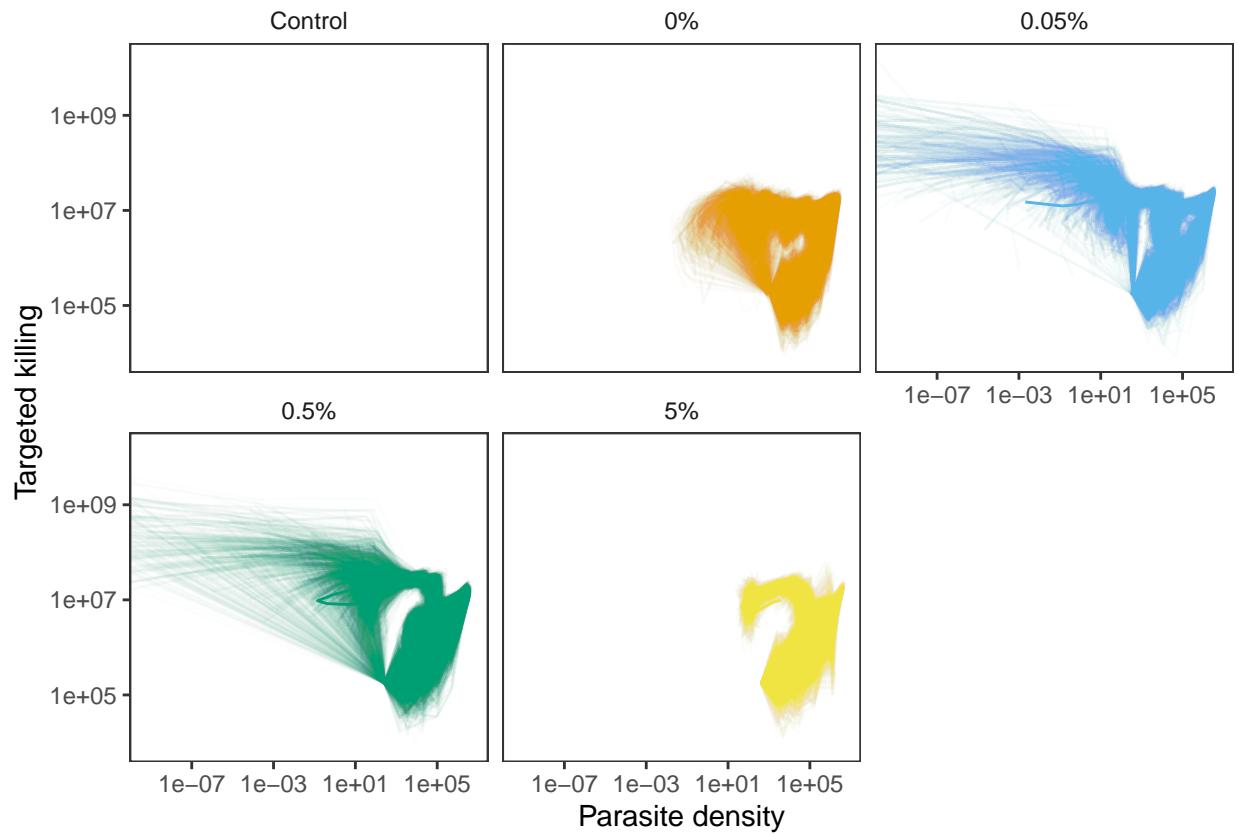


Read in data of weighted individual trajectories

```
## Rows: 606492 Columns: 11
## -- Column specification --
## Delimiter: ","
## chr (2): box, mouse
## dbl (9): rep, time, E, R, W, N, K, lik, rep2
##
## i Use `spec()` to retrieve the full column specification for this data.
## i Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

Plot individual weighted trajectories with group-level trajectories

```
## Warning: Transformation introduced infinite values in continuous x-axis
## Warning: Transformation introduced infinite values in continuous y-axis
## Warning: Transformation introduced infinite values in continuous x-axis
## Warning: Removed 26 rows containing missing values ('geom_path()').
```



```
## Warning: Transformation introduced infinite values in continuous y-axis
## Removed 26 rows containing missing values ('geom_path()').
```

