

Mediation test on natural isolates. short version

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June 13, 2017

```
rm(list=ls())
#setwd("~/github/0.network.aging.prj.bmc/0a.rls.fitting")
setwd("~/github/bmc_netwk_aging_manuscript/R1/0.nat.rls.fitting")
library('flexsurv')
```

```
## Loading required package: survival
```

```
source("../lifespan.r")
```

Parse strains from files

```
files = list.files(path="../qinlab_rls/", pattern="rls.tab")
tmp1 = gsub("\\d{6}.", "", files)
redundant_strains = gsub(".rls.tab", "", tmp1)
strains = sort( unique( redundant_strains ) )
strains
```

```
## [1] "101S"          "BY4716"          "BY4741"          "BY4742"
## [5] "BY4743"        "JSBY4741"        "M1-2"            "M13"
## [9] "M14"           "M2-8"            "M22"             "M32"
## [13] "M34"           "M5"              "M8"              "RM112N"
## [17] "S288c"         "SGU57"           "sir2D.4741a"     "sir2D.4742"
## [21] "sir2DSIR2.4742" "SK1"             "W303"            "YPS128"
## [25] "YPS163"
```

Take files from natural isolates

```
my.strains=c("101S", "M1-2", "M13", "M14", "M2-8", "M22", "M32", "M34", "M5", "M8", "RM112N", "S288c", "SGU57", "YPS163")
files2=c();
for( i in 1:length(my.strains)){
  files2 = c( files2, files[grep(my.strains[i], files)]);
}

report = data.frame(cbind(my.strains))
report$samplesize = NA; report$R=NA; report$t0=NA; report$n=NA; report$G=NA; report$longfilename=NA;

files = files2;
strains = my.strains;
```

Now, fit all RLS data sets by strains

```
for( i in 1:length(report[,1])){
  #for( i in 3:4){
    my.files = files[grep(strains[i], files)]
```

```

report$longfilename[i] = paste(my.files, collapse = "::");
tb = read.table( paste("../qinlab_rls/",my.files[1],sep=''), sep="\t")
if( length(my.files)> 1){
  for( fi in 2:length(my.files)) {
    tmp.tb = read.table( paste("../qinlab_rls/",my.files[fi],sep=''), sep="\t")
    tb = rbind( tb, tmp.tb)
  }
}
report$samplesize[i] = length(tb[,1])

GompFlex = flexsurvreg(formula = Surv(tb[,1]) ~ 1, dist = 'gompertz')
WeibFlex = flexsurvreg(formula = Surv(tb[,1]) ~ 1, dist = 'weibull')

report$avgLS[i] = mean(tb[,1])
report$stdLS[i] = sd(tb[,1])
report$CV[i] = report$stdLS[i] / report$avgLS[i]

report$GompGFlex[i] = GompFlex$res[1,1]
report$GompRFlex[i] = GompFlex$res[2,1]
report$GompLogLikFlex[i] = round(GompFlex$loglik, 1)
report$GompAICFlex[i] = round(GompFlex$AIC)

report$WeibShapeFlex[i] = WeibFlex$res[1,1]
report$WeibRateFlex[i] = WeibFlex$res[2,1]
report$WeibLogLikFlex[i] = round(WeibFlex$loglik, 1)
report$WeibAICFlex[i] = round(WeibFlex$AIC)

#set initial values
Rhat = report$GompRFlex[i]; # 'i' was missing. a bug costed HQ a whole afternoon.
Ghat = report$GompGFlex[i];
nhathat = 6;
t0= (nhathat-1)/Ghat;
fitBinom = optim ( c(Rhat, t0, nhathat), llh.binomialMortality.single.run,
                  lifespan=tb[,1],
                  #method='SANN') #SANN needs control
                  method="L-BFGS-B",
                  lower=c(1E-10, 1, 4), upper=c(1,200,20) );
report[i, c("R", "t0", "n")] = fitBinom$par[1:3]
report$G[i] = (report$n[i] - 1)/report$t0[i]
}
report2 = report;

```

Mediation test on Gflex \leftarrow t0 \leftarrow RFlex

Hong thinks the results indicate the t0 is the mediator from Flex to GFlex, but not sure.

```
library(mediation)
```

```
## Loading required package: MASS
```

```

## Loading required package: Matrix
## Loading required package: mvtnorm
## Loading required package: sandwich
## mediation: Causal Mediation Analysis
## Version: 4.4.5
set.seed(20170801)
report2$log10GompRFlex = log10(report2$GompRFlex)
med.fit = lm(t0 ~ log10GompRFlex, data=report2)
summary(med.fit)

##
## Call:
## lm(formula = t0 ~ log10GompRFlex, data = report2)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -10.2238  -7.6956  -0.6106   1.5195  22.5871
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    99.564     20.269   4.912 0.000284 ***
## log10GompRFlex  19.967       7.429   2.688 0.018617 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 9.928 on 13 degrees of freedom
## Multiple R-squared:  0.3572, Adjusted R-squared:  0.3078
## F-statistic: 7.225 on 1 and 13 DF,  p-value: 0.01862
out.fit = lm(GompGFlex ~ t0 + log10GompRFlex, data=report2)
summary(out.fit)

##
## Call:
## lm(formula = GompGFlex ~ t0 + log10GompRFlex, data = report2)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.008037 -0.004385 -0.001282  0.001773  0.012763
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)    0.1818701  0.0236582   7.687 5.64e-06 ***
## t0             -0.0020169  0.0001916 -10.529 2.05e-07 ***
## log10GompRFlex -0.0095046  0.0063994  -1.485   0.163
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 0.006857 on 12 degrees of freedom
## Multiple R-squared:  0.9447, Adjusted R-squared:  0.9355
## F-statistic: 102.5 on 2 and 12 DF,  p-value: 2.861e-08

```

```
med.out <- mediate(med.fit, out.fit, treat = "log10GompRFlex", mediator = "t0", robustSE = TRUE, sims =
summary(med.out)
```

```
##
## Causal Mediation Analysis
##
## Quasi-Bayesian Confidence Intervals
##
##           Estimate 95% CI Lower 95% CI Upper p-value
## ACME           -0.04383    -0.08096    -0.01  <2e-16 ***
## ADE            -0.00718    -0.02469     0.01   0.46
## Total Effect   -0.05101    -0.08276    -0.02  <2e-16 ***
## Prop. Mediated  0.86767     0.46191     1.23  <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Sample Size Used: 15
##
##
## Simulations: 100
```

Mediation test 2 on Rflex \leftarrow t0 \leftarrow GFlex

Hong thinks this is negative result, which means t0 works only in one direction.

```
med.fit = lm(t0 ~ GompGFlex, data=report2)
summary(med.fit)
```

```
##
## Call:
## lm(formula = t0 ~ GompGFlex, data = report2)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -2.6401 -1.9424 -0.8670 -0.0658  8.1513
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)   94.999      3.723   25.52 1.72e-12 ***
## GompGFlex    -427.325     31.369  -13.62 4.50e-09 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.168 on 13 degrees of freedom
## Multiple R-squared:  0.9345, Adjusted R-squared:  0.9295
## F-statistic: 185.6 on 1 and 13 DF,  p-value: 4.503e-09

out.fit = lm(log10GompRFlex ~ t0 + GompGFlex, data=report2)
summary(out.fit)
```

```
##
## Call:
## lm(formula = log10GompRFlex ~ t0 + GompGFlex, data = report2)
##
## Residuals:
##      Min       1Q   Median       3Q      Max
## -0.52342 -0.24509  0.04331  0.22083  0.34492
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  -0.002954   2.387477  -0.001   0.999
## t0            -0.017838   0.024884  -0.717   0.487
## GompGFlex    -16.337520  10.999937  -1.485   0.163
##
## Residual standard error: 0.2843 on 12 degrees of freedom
## Multiple R-squared:  0.457, Adjusted R-squared:  0.3666
## F-statistic: 5.051 on 2 and 12 DF,  p-value: 0.02562
med.out <- mediate(med.fit, out.fit, treat = "GompGFlex", mediator = "t0", robustSE = TRUE, sims = 100)
summary(med.out)

##
## Causal Mediation Analysis
##
## Quasi-Bayesian Confidence Intervals
##
##              Estimate 95% CI Lower 95% CI Upper p-value
## ACME              6.454    -14.468     31.46   0.74
## ADE             -15.052    -45.810      8.83   0.18
## Total Effect     -8.598    -18.553     -1.06   0.04 *
## Prop. Mediated   -0.526     -9.794      3.54   0.74
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Sample Size Used: 15
##
##
## Simulations: 100
```