A basic semicompeting risks model in Stan

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Model formulation

Weibull models

The hazard of a Weibull regression model with shape α is

$$h(t|x_i) = \alpha t^{\alpha-1} \exp\{x_i'\beta\}$$

With $\kappa = \exp(\beta_0)$, this is the parameterization used in Lee et al.

Alternatively, one can use the Stan hazard parameterization, where

$$h(t) = \frac{\alpha}{\sigma}\left(\frac{t}{\sigma}\right)^{\alpha-1}$$

To incorporate regression parameters into the model, we note that

$$\sigma^{-\alpha} = \exp\{x_i'\beta\}$$

and thus

$$\sigma = \exp\left\{-\frac{x_i'\beta}{\alpha}\right\}$$

Likelihood contributions by observed data pattern

TODO(LCOMM): Type out likelihood

Observed

TODO(LCOMM): Observed data pattern table

TODO(LCOMM): Likelihood contributions by data pattern

```r
# Packages
suppressPackageStartupMessages(library("rstan"))
rstan_options(auto_write = TRUE)
options(mc.cores = parallel::detectCores() - 1)
```

```r
# Read in semicompeting risk Weibull simulated data
dat_ID <- readRDS("dat_ID.Rdata")

# Package for Stan
x_m <- cbind(1, dat_ID$x_c)
stan_dat <-  list(N = nrow(dat_ID),
                  P_1 = ncol(x_m),
                  X_1 = x_m,
                  P_2 = ncol(x_m),
```

```
                  X_2 = x_m,
                  P_3 = ncol(x_m),
                  X_3 = x_m,
                  Yr = dat_ID$R,
                  dYr = dat_ID$delta_R,
                  Yt = dat_ID$T,
                  dYt = dat_ID$delta_T)
```

The Stan code to fit these models is shown below.

```
data {
  // number of observations
  int<lower=0> N;
  // number of columns in 1st design matrix, including intercept
  int<lower=1> P_1;
  // design matrix for non-terminal model
  matrix[N, P_1] X_1;
  // number of columns in 2nd design matrix, including intercept
  int<lower=1> P_2;
  // design matrix for terminal model w/o non-terminal history
  matrix[N, P_2] X_2;
  // number of columns in 3rd design matrix, including intercept
  int<lower=1> P_3;
  // design matrix for terminal model with non-terminal history
  matrix[N, P_3] X_3;
  // observed non-terminal time
  vector<lower=0>[N] Yr;
  // indicator of event observation for non-terminal event
  int<lower=0,upper=1> dYr[N];
  // observed terminal time
  vector<lower=0>[N] Yt;
  // indicator of event observation for terminal event
  int<lower=0,upper=1> dYt[N];
}

transformed data {
  // Duration of gap between non-terminal and terminal events
  vector[N] YtYrdiff;
  YtYrdiff = Yt - Yr;
}

parameters {
  // vectors of regression parameters
  vector[P_1] beta1;
  vector[P_2] beta2;
  vector[P_3] beta3;

  // shape parameters (the one in exponent of time)
  // alpha > 1 -> hazard increases over time, more clumping
  real<lower=0> alpha1;
  real<lower=0> alpha2;
  real<lower=0> alpha3;

  // scale parameters
```

```
  // bigger sigma -> slower event occurrence (double check this)
  //real<lower=0> sigma1;
  //real<lower=0> sigma2;
  //real<lower=0> sigma3;
}

model {
  // linear predictors
  vector[N] lp1;
  vector[N] lp2;
  vector[N] lp3;
  lp1 = X_1 * beta1;
  lp2 = X_2 * beta2;
  lp3 = X_3 * beta3;

  // no priors -> use Stan defaults

  // likelihood
  for (n in 1:N){
    if (dYr[n] == 0 && dYt[n] == 0) {

      // type 1: observe neither event
      target += weibull_lccdf(Yr[n] | alpha1, exp(-(lp1[n])/alpha1)) +
                weibull_lccdf(Yt[n] | alpha2, exp(-(lp2[n])/alpha2));

    } else if (dYr[n] == 1 && dYt[n] == 0) {

      // type 2: observe non-terminal but terminal censored
      target += weibull_lpdf(Yr[n] | alpha1, exp(-(lp1[n])/alpha1)) +
                weibull_lccdf(Yr[n] | alpha2, exp(-(lp2[n])/alpha2)) +
                weibull_lccdf(YtYrdiff[n] | alpha3, exp(-(lp3[n])/alpha3));

    } else if (dYr[n] == 0 && dYt[n] == 1) {

      // type 3: observed terminal with no prior non-terminal
      target += weibull_lccdf(Yr[n] | alpha1, exp(-(lp1[n])/alpha1)) +
                weibull_lpdf(Yt[n] | alpha2, exp(-(lp2[n])/alpha2));

    } else if (dYr[n] == 1 && dYt[n] == 1) {

      // type 4: both non-terminal and terminal observed
      target += weibull_lpdf(Yr[n] | alpha1, exp(-(lp1[n])/alpha1)) +
                weibull_lccdf(Yr[n] | alpha2, exp(-(lp2[n])/alpha2)) +
                weibull_lpdf(YtYrdiff[n] | alpha3, exp(-(lp3[n])/alpha3));

    }
  }
}
```

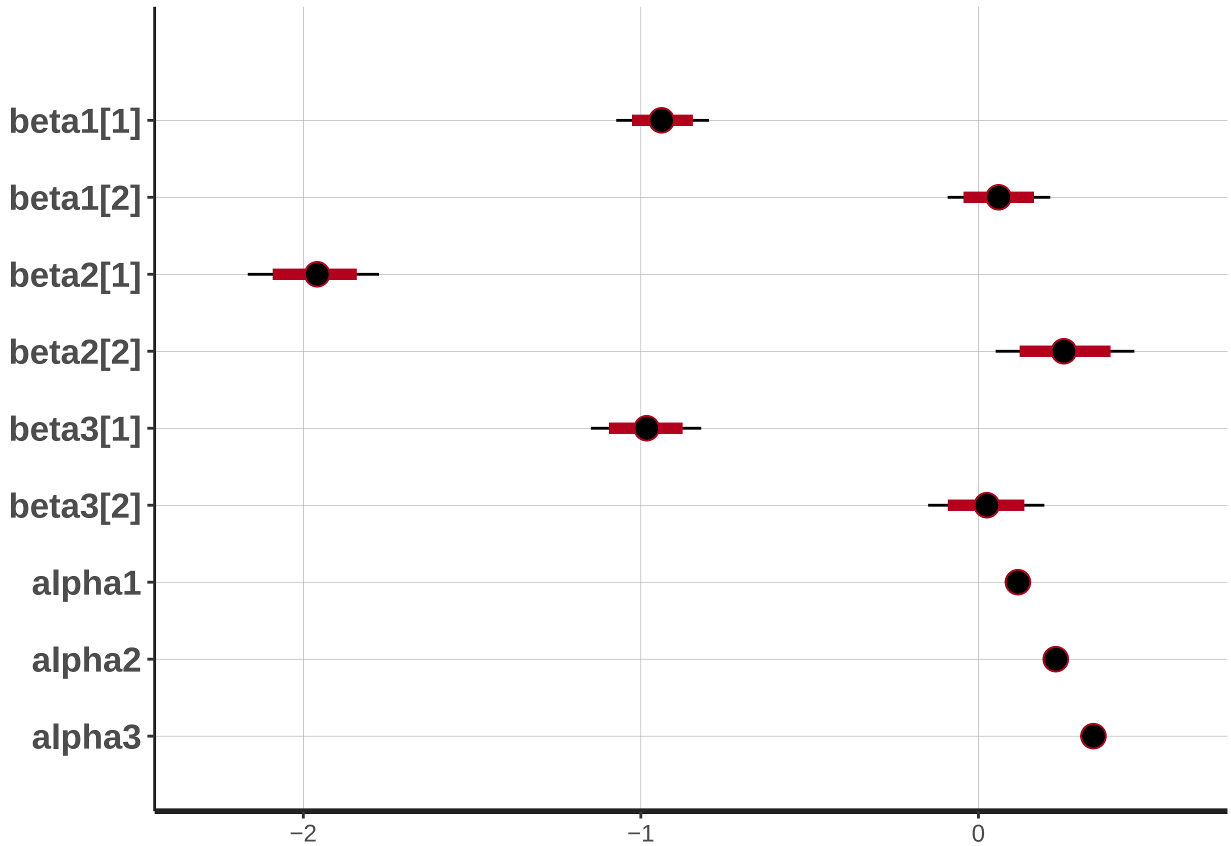
```
# Fit Weibull semicompeting model
library("rstan")
fit1 <- stan(file = "semicompeting_weibull.stan", data = stan_dat,
             iter = 1000, chains = 4)
summary(fit1)[["summary"]]
```

```
##                  mean     se_mean          sd          2.5%
## beta1[1] -9.386601e-01 1.561794e-03 0.069845551 -1.072907e+00
## beta1[2]  6.035495e-02 1.791009e-03 0.080096346 -9.133991e-02
## beta2[1] -1.962410e+00 2.227488e-03 0.098383963 -2.164367e+00
## beta2[2]  2.543048e-01 2.354872e-03 0.105313064  5.055478e-02
## beta3[1] -9.844034e-01 1.898033e-03 0.084882608 -1.147983e+00
## beta3[2]  2.302398e-02 1.987692e-03 0.088892270 -1.489141e-01
## alpha1    1.168827e-01 8.775352e-05 0.003924457  1.091760e-01
## alpha2    2.289271e-01 2.120797e-04 0.009484491  2.104455e-01
## alpha3    3.407741e-01 2.439019e-04 0.010907624  3.196419e-01
## lp__     -3.214298e+03 6.978859e-02 2.057081446 -3.219054e+03
##                   25%           50%           75%         97.5%     n_eff
## beta1[1] -9.843496e-01 -9.390387e-01 -8.918447e-01    -0.7984249 2000.0000
## beta1[2]  4.356931e-03  5.990967e-02  1.137667e-01     0.2127391 2000.0000
## beta2[1] -2.029885e+00 -1.958928e+00 -1.893099e+00    -1.7748420 1950.8231
## beta2[2]  1.817880e-01  2.529893e-01  3.270500e-01     0.4617319 2000.0000
## beta3[1] -1.042230e+00 -9.829984e-01 -9.251052e-01    -0.8212657 2000.0000
## beta3[2] -3.818477e-02  2.470272e-02  8.395738e-02     0.1957215 2000.0000
## alpha1    1.142895e-01  1.168423e-01  1.194361e-01     0.1248782 2000.0000
## alpha2    2.225156e-01  2.289380e-01  2.351512e-01     0.2476558 2000.0000
## alpha3    3.336239e-01  3.405563e-01  3.478461e-01     0.3626364 2000.0000
## lp__     -3.215470e+03 -3.213951e+03 -3.212786e+03 -3211.2691786  868.8286
##               Rhat
## beta1[1] 0.9995252
## beta1[2] 0.9994217
## beta2[1] 1.0021486
## beta2[2] 1.0008264
## beta3[1] 1.0014051
## beta3[2] 1.0001848
## alpha1   0.9981954
## alpha2   0.9991849
## alpha3   1.0001593
## lp__     1.0043064
```

```r
plot(fit1)
```

```
## ci_level: 0.8 (80% intervals)
```

```
## outer_level: 0.95 (95% intervals)
```



TODO(LCOMM): Look into reparameterization to reduce numerical issues

```
# Compare to Lee et al
library("SemiCompRisks")
```

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

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

```
# Objects
Y = data.frame(dat_ID$R, dat_ID$delta_R,
               dat_ID$T, dat_ID$delta_T)
lin.pred = list(formula(~ x_c),
                formula(~ x_c),
                formula(~ x_c))

### Hyperparameters
## Subject-specific frailty variance component
##  - prior parameters for 1/theta
theta.ab <- c(0.7, 0.7)

## Weibull baseline hazard function: alphas, kappas
WB.ab1 <- c(0.5, 0.01) # prior parameters for alpha1
WB.ab2 <- c(0.5, 0.01) # prior parameters for alpha2
WB.ab3 <- c(0.5, 0.01) # prior parameters for alpha3
##
WB.cd1 <- c(0.5, 0.05) # prior parameters for kappa1
WB.cd2 <- c(0.5, 0.05) # prior parameters for kappa2
WB.cd3 <- c(0.5, 0.05) # prior parameters for kappa3
```

```r
hyperParams <- list(theta = theta.ab,
                    WB = list(WB.ab1 = WB.ab1, WB.ab2 = WB.ab2, WB.ab3 = WB.ab3,
                              WB.cd1 = WB.cd1, WB.cd2 = WB.cd2, WB.cd3 = WB.cd3))

###################
## MCMC SETTINGS ##
###################

## Setting for the overall run
numReps    <- 5000
thin       <- 10
burninPerc <- 0.6

## Settings for storage
nGam_save <- 0
storeV    <- rep(TRUE, 3)

## Tuning parameters for specific updates
mhProp_theta_var  <- 0.05
mhProp_Vg_var     <- c(0.05, 0.05, 0.05)

## Specific to the Weibull specification of the baseline hazard functions
mhProp_alphag_var <- c(0.01, 0.01, 0.01)
mcmc.WB  <- list(run = list(numReps = numReps, thin = thin, burninPerc = burninPerc),
                 storage = list(nGam_save = nGam_save, storeV=storeV),
                 tuning = list(mhProp_theta_var = mhProp_theta_var,
                               mhProp_Vg_var = mhProp_Vg_var,
                               mhProp_alphag_var = mhProp_alphag_var))
myModel <- c("semi-Markov", "Weibull")
startValues      <- vector("list", 2)
startValues[[1]] <- initiate.startValues_HReg(Y, lin.pred, dat_ID, model = myModel)
```

```
##
## [1] "Start values are initiated for semi-competing risks Weibull model..."
```

```r
startValues[[2]] <- initiate.startValues_HReg(Y, lin.pred, dat_ID, model = myModel,
                                              theta = 0.23)
```

```
##
## [1] "Start values are initiated for semi-competing risks Weibull model..."
```

```r
startValues[[3]] <- initiate.startValues_HReg(Y, lin.pred, dat_ID, model = myModel,
                                              theta = 0.72)
```

```
##
## [1] "Start values are initiated for semi-competing risks Weibull model..."
```

```r
startValues[[4]] <- initiate.startValues_HReg(Y, lin.pred, dat_ID, model = myModel,
                                              theta = 0.55)
```

```
##
## [1] "Start values are initiated for semi-competing risks Weibull model..."
```

```r
# Fit SemiCompRisks models
fit2 <- BayesID_HReg(Y, lin.pred, data = dat_ID,
                     hyperParams = hyperParams, startValues = startValues,
```

```r
                      mcmc = mcmc.WB, path = "SemiCompRisks/Output/")
```

```
## chain:  1
## chain:  2
## chain:  3
## chain:  4
```

```r
print(fit2)
```

```
##
## Analysis of independent semi-competing risks data
## semi-Markov assumption for h3
##
## Number of chains:     4
## Number of scans:      5000
## Thinning:             10
## Percentage of burnin: 60%
##
## ######
## Potential Scale Reduction Factor
##
## Variance of frailties, theta:
##  2.338
##
## Regression coefficients:
##     beta1 beta2 beta3
## x_c 1.094 1.059 1.037
##
## Baseline hazard function components:
##          h1    h2    h3
## kappa 1.004 1.065 1.090
## alpha 1.289 1.197 1.442
##
## ######
## Estimates
##
## Variance of frailties, theta:
##  Estimate    SD    LL  UL
##     0.233 0.076 0.118 0.4
##
## Regression coefficients:
##     Estimate    SD    LL    UL
## x_c    0.049 0.095 0.869 1.244
## x_c    0.245 0.117 1.075 1.675
## x_c    0.041 0.113 0.809 1.248
```

```r
str(summary(fit2))
```

```
## List of 6
##  $ classFit: chr [1:4] "Bayes_HReg" "ID" "Ind" "WB"
##  $ psrf    :List of 3
##   ..$ theta: num [1, 1] 2.34
##   .. ..- attr(*, "dimnames")=List of 2
##   .. .. ..$ : chr ""
##   .. .. ..$ : chr ""
```

```
##   ..$ coef : num [1, 1:3] 1.09 1.06 1.04
##   .. ..- attr(*, "dimnames")=List of 2
##   .. .. ..$ : chr "x_c"
##   .. .. ..$ : chr [1:3] "beta1" "beta2" "beta3"
##   ..$ h0   : num [1:2, 1:3] 1 1.29 1.06 1.2 1.09 ...
##   .. ..- attr(*, "dimnames")=List of 2
##   .. .. ..$ : chr [1:2] "kappa" "alpha"
##   .. .. ..$ : chr [1:3] "h1" "h2" "h3"
##  $ theta   : num [1, 1:3] 0.233 0.118 0.4
##   ..- attr(*, "dimnames")=List of 2
##   .. ..$ : chr ""
##   .. ..$ : chr [1:3] "theta" "LL" "UL"
##  $ coef    : num [1, 1:9] 1.05 0.869 1.244 1.278 1.075 ...
##   ..- attr(*, "dimnames")=List of 2
##   .. ..$ : chr "x_c"
##   .. ..$ : chr [1:9] "exp(beta1)" "LL" "UL" "exp(beta2)" ...
##  $ h0      : num [1:2, 1:9] -2.079 -0.842 -2.134 -0.992 -2.026 ...
##   ..- attr(*, "dimnames")=List of 2
##   .. ..$ : chr [1:2] "Weibull: log-kappa" "Weibull: log-alpha"
##   .. ..$ : chr [1:9] "h1-PM" "LL" "UL" "h2-PM" ...
##  $ setup   :List of 12
##   ..$ nCov       : int [1:3] 1 1 1
##   ..$ hyperParams: num [1:14] 0.5 0.01 0.5 0.01 0.5 0.01 0.5 0.05 0.5 0.05 ...
##   ..$ startValues:List of 4
##   .. ..$ :List of 2
##   .. .. ..$ common:List of 5
##   .. .. .. ..$ beta1   : num 0.0121
##   .. .. .. ..$ beta2   : num -0.0126
##   .. .. .. ..$ beta3   : num 0.0168
##   .. .. .. ..$ gamma.ji: num [1:1500] 0.399 0.124 0.335 0.03 1.486 ...
##   .. .. .. ..$ theta   : num 1.06
##   .. .. ..$ WB    :List of 2
##   .. .. .. ..$ WB.alpha: num [1:3] 1 1 1
##   .. .. .. ..$ WB.kappa: num [1:3] 0.01 0.01 0.01
##   .. ..$ :List of 2
##   .. .. ..$ common:List of 5
##   .. .. .. ..$ beta1   : num 0.0661
##   .. .. .. ..$ beta2   : num 0.0118
##   .. .. .. ..$ beta3   : num -0.0658
##   .. .. .. ..$ gamma.ji: num [1:1500] 0.849 0.676 0.844 0.805 0.719 ...
##   .. .. .. ..$ theta   : num 0.23
##   .. .. ..$ WB    :List of 2
##   .. .. .. ..$ WB.alpha: num [1:3] 1 1 1
##   .. .. .. ..$ WB.kappa: num [1:3] 0.01 0.01 0.01
##   .. ..$ :List of 2
##   .. .. ..$ common:List of 5
##   .. .. .. ..$ beta1   : num 0.0401
##   .. .. .. ..$ beta2   : num -0.0243
##   .. .. .. ..$ beta3   : num 0.0623
##   .. .. .. ..$ gamma.ji: num [1:1500] 1.7153 0.8886 0.0485 0.4012 0.6849 ...
##   .. .. .. ..$ theta   : num 0.72
##   .. .. ..$ WB    :List of 2
##   .. .. .. ..$ WB.alpha: num [1:3] 1 1 1
##   .. .. .. ..$ WB.kappa: num [1:3] 0.01 0.01 0.01
```

```
##   .. ..$ :List of 2
##   .. .. ..$ common:List of 5
##   .. .. .. ..$ beta1   : num 0.0288
##   .. .. .. ..$ beta2   : num 0.0623
##   .. .. .. ..$ beta3   : num -0.0032
##   .. .. .. ..$ gamma.ji: num [1:1500] 1.069 0.645 0.725 2.669 1.621 ...
##   .. .. .. ..$ theta   : num 0.55
##   .. .. ..$ WB    :List of 2
##   .. .. .. ..$ WB.alpha: num [1:3] 1 1 1
##   .. .. .. ..$ WB.kappa: num [1:3] 0.01 0.01 0.01
##   ..$ mcmcParams : num [1:4] 0.01 0.01 0.01 0.05
##   ..$ nGam_save  : num 0
##   ..$ numReps    : num 5000
##   ..$ thin       : num 10
##   ..$ path       : chr "SemiCompRisks/Output/"
##   ..$ burninPerc : num 0.6
##   ..$ hz.type    : chr "Weibull"
##   ..$ model      : chr "semi-Markov"
##   ..$ nChain     : int 4
##  - attr(*, "class")= chr "summ.Bayes_HReg"
```

```r
theta_est <- summary(fit2)[["theta"]][,1]
kappa_ests <- exp(summary(fit2)[["h0"]][1, c(1,4,7)])
beta0_ests <- summary(fit2)[["h0"]][1, c(1,4,7)]
alpha_ests <- exp(summary(fit2)[["h0"]][2, c(1,4,7)])
beta_ests <- log(summary(fit2)[["coef"]][c(1,4,7)])

# print(fit2)
# str(summary(fit2)$psrf)
# plot(fit2)
# str(fit2)
#
# # Extract comparable to Stan output
# beta01 <- log(summary(fit2)[["psrf"]][["h0"]]["kappa","h1"])
# beta02 <- log(summary(fit2)[["psrf"]][["h0"]]["kappa","h2"])
# beta03 <- log(summary(fit2)[["psrf"]][["h0"]]["kappa","h3"])
# beta_x <- summary(fit2)[["psrf"]][["coef"]]
```

TODO(LCOMM): Finish comparison table