

# Prediction in Joint Models

## 1 Description

This method is the Python adaptation of R's `survfitJM` function. It computes  $\pi(s + t|s)$  the probability at time  $s$  of surviving over time  $s+t$ .

The probability for a subject  $i$  we know alive at time  $s$  to survive over time  $s + t$  can be formulated by the following formula :

$$\begin{aligned}\pi_i(s + t|s) &= \mathbb{P}(T_i^* \geq s + t | T_i^* > s, \mathcal{Y}_i(s); \theta) \\ &= \int \frac{S_i(s + t | \mathcal{M}_i(s + t, b_i, \theta); \theta)}{S_i(s | \mathcal{M}_i(s, b_i, \theta); \theta)} * p(b_i | T_i^* > s, \mathcal{Y}_i(s); \theta) db_i\end{aligned}$$

Where the different terms denotes :

- $\pi_i(x)$  : Probability for subject  $i$  to be alive at time  $x$
- $s$  : time from when we know or we assume the subject is alive and from when we want to compute predictions of his future survival probabilities
- $t$  : time horizon from  $s$ . The survival probability is given for time  $s + t$
- $T_i^*$  : Random variable representing time when subject  $i$  dies
- $\mathcal{Y}_i(x)$  : Longitudinal measurement of subject  $i$  before time  $x$
- $\theta$  : Parameters of joint model
- $S_i()$  : Survival function of subject  $i$
- $\mathcal{M}_i()$  : Longitudinal history of subject  $i$ , approximated by the linear mixed-effects model
- $b_i$  : Subject  $i$  random effects

## 2 Usage

Call `.Survfit()`

Once your JointModel object is fitted, call `object.Survfit(new_data, id_var)`. `new_data` and `id_var` are the only required arguments. The other arguments are optional.

#### Default values

- `surv_times` = None
- `last_time` = None
- `ci` = `numpy.array([0.025, 0.975])`
- `M` = 200
- `scale` = 1.6
- `simulate` = False

### 3 Arguments

- `new_data` : A pandas dataframe containing covariates used in both survival and linear mixed-effects models and longitudinal information ordered by increasing time for each subject. `new_data` must also contain a column that identifies different subjects. The names of covariates columns must be the same in `new_data` and in data used to fit the model. This dataframe is structured with one line for each longitudinal information. It could contain information for several subjects. An example of a valid `new_data` is provided just below

id_subject	longitudinal var	Linear var 1	Surv var 1	Surv var 2
1	221	12	58	0
1	257	24	58	0
1	284	36	58	0
2	112	14	65	1
2	191	26	65	1

- `id_var` : Name of the column that identifies subjects in `new_data`.
- `surv_times` : Numerical numpy array containing one or several times  $s + t$  of predictions. If `surv_times` is None,  $s + t$  will be automatically generated.
- `last_time` :  $s$  time from when we know or assume a subject is alive and from when we want to predict at time  $s + t$ . `last_time` could be a character string or a numeric numpy array. If `last_time` is a string, the name of a column in `new_data` containing  $s$  time from which we predict is expected in input. If `last_time` is a numpy array, it must be a vector containing  $s$  time for each subject. If `last_time` is None, last longitudinal time in `new_data` will be taken as `last_time`. **Warning** each subject must have only one  $s$  time.
- `ci` : Numerical numpy array that specifies which quantiles to use for the computation of confidence interval for the predicted probabilities.

- $M$  : Integer denoting how many loop are computed in Monte-Carlo method to estimate survival probabilities and compute a confidence interval.
- $scale$  : A numeric scalar that controls the acceptance rate of the Metropolis-Hastings algorithm
- $simulate$  : A boolean (True or False) that specifies if we estimate our survival probabilities using Monte-Carlo method or not. If  $simulate$  is True, survival probabilities will be computed by a Monte-Carlo method and a confidence interval will be provided. If  $simulate$  is False, probabilities will be computed without Monte-Carlo method and only ponctual estimation will be return.

## 4 Details

Estimation of  $\pi_i(s + t|s)$  computation method will depend on  $simulate$  argument.

**simulate = True** Estimation will be based on following Monte-Carlo procedure :

**Step1** : Simulate  $\theta^{(l)}$  vector of parameters values from a multivariate normal distribution  $\mathcal{N}(\hat{\theta}, C(\hat{\theta}))$  where  $\hat{\theta}$  are the fitted joint model's parameters estimated by MLE and  $C(\hat{\theta})$  their variance-covariance matrix.

**Step2** : Simulate  $b_i^{(l)}$  random effects of subject  $i$  from  $b_i$  posterior distribution given  $T_i^* > s$ ,  $\mathcal{Y}_i(s)$  and  $\theta^{(l)}$ . This is achieved using a Metropolis-Hastings algorithm with independent proposals from a properly centered and scaled multivariate t distribution. The  $scale$  argument controls the acceptance rate for this algorithm.

**Step3** : Compute:

$$\pi_i^{(l)}(s + t|s) = \frac{S_i(s + t|\mathcal{M}_i(s + t, b_i^{(l)}, \theta^{(l)}); \theta^{(l)})}{S_i(s|\mathcal{M}_i(s, b_i^{(l)}, \theta^{(l)}); \theta^{(l)})}$$

Steps 1-3 are repeated  $l = 1, \dots, M$  times M is given by  $M$  argument of *Survfit()* method.

**simulate = False** Survival probabilities will be estimated by :

$$\tilde{\pi}_i(s + t|s) = \frac{S_i(s + t|\mathcal{M}_i(s + t, \hat{b}_i^{(s)}, \hat{\theta}); \hat{\theta})}{S_i(s|\mathcal{M}_i(s, \hat{b}_i^{(s)}, \hat{\theta}); \hat{\theta})}$$

Where the different terms denotes :

- $\tilde{\pi}_i(x)$  : Estimated probability for subject  $i$  to be alive at time  $x$

- $s$  : time from when we know or we assume the subject is alive and from when we want to compute predictions of his future survival probabilities
- $t$  : time horizon from  $s$ . The survival probability is given for time  $s + t$
- $\hat{\theta}$  : MLE of parameters of joint model
- $\hat{b}_i^{(s)}$  : Mode of the conditional distribution  $p(b_i | T_i^* > s, \mathcal{Y}_i(s); \hat{\theta})$
- $S_i()$  : Survival function of subject  $i$
- $\mathcal{M}_i()$  : Longitudinal history of subject  $i$ , approximated by the linear mixed-effects model

## 5 Value

A dictionary containing a pandas dataframe for each group inputed in *new\_data*. Each dataframe provide estimated probabilities to survive at each  $s + t$  times. If *simulate* is True, the returned dataframe will contain a summary of  $M$  predictions containing : mean, median, low and high boundaries of confidence interval. And if *simulate* is False, only ponctual estimation will be returned.

## 6 References

Rizopoulos, D. (2012) *Joint Models for Longitudinal and Time-to-Event Data: with Applications in R*. Boca Raton: Chapman and Hall/CRC.