Building augmented data for multi-state models: the msmtools package version 1.2

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1 Introduction

Package msmtools is an R package whose main goal is to facilitate the workflow with longitudinal datasets which need to be analyzed in the context of multi-state models. In particular, msmtools acts as the msm package companion (Jackson 2011). Moreover, msmtools is focused on efficiency and speed, also thanks to package data.table (Dowle et al. 2014).

1.1 Longitudinal Dataset

Everytime we observe a given subject multiple times, we come up with a longitudinal dataset. This means that measures are repeated n times in a sequence which, in general, may not be equal for all the subjects. Moreover, a longitudinal dataset could be viewed as a multilevel

dataset: a first level is given by the subject, and a second level is given by the single observation carried out on that subject. A very common case of longitudinal dataset deals with hospital admissions. A patient, our subject, can have a series of entries which correspond to hospital admissions. Each hospital admission is recorded in a single row of the dataset. Let's consider a simplified version of the hosp dataset which comes with msmtools package and represents synthetic hospital admissions for 10 patients. For a detailed description of the dataset, please run ?hosp. For demonstration purposes, we extract only the first 2 patients, reducing the hosp dataset to a test sample of 17 rows per 8 variables as you can see below.

```
data( hosp )
hosp[1:17, .( subj, adm number, gender, age, label 2,
                dateIN, dateOUT, dateCENS ) ]
##
       subj adm number gender age label 2
                                                 dateIN
                                                            dateOUT
                                                                       dateCENS
##
    1:
          1
                      1
                              F
                                 83
                                        dead 2008-11-30 2008-12-12 2011-04-28
##
    2:
          1
                      2
                              F
                                 83
                                        dead 2009-01-26 2009-02-16 2011-04-28
                      3
                              F
##
    3:
          1
                                 83
                                        dead 2009-05-13 2009-05-15 2011-04-28
##
    4:
                      4
                              F
                                 83
                                        dead 2009-05-20 2009-05-25 2011-04-28
          1
                      5
    5:
                              F
                                 83
                                        dead 2009-06-12 2009-06-16 2011-04-28
##
          1
##
    6:
          1
                      6
                              F
                                 83
                                        dead 2009-06-20 2009-06-25 2011-04-28
    7:
                      7
                              F
                                 83
                                        dead 2009-07-17 2009-07-22 2011-04-28
##
          1
##
    8:
          1
                      8
                              F
                                 84
                                        dead 2010-04-15 2010-04-20 2011-04-28
    9:
                      9
                              F
                                        dead 2010-10-11 2010-10-14 2011-04-28
##
          1
                                 84
                                        dead 2011-01-14 2011-01-17 2011-04-28
## 10:
          1
                     10
                              F
                                 85
## 11:
                              F
                                        dead 2011-04-27 2011-04-28 2011-04-28
          1
                     11
                                 85
## 12:
          2
                              F
                                 99
                                       alive 2007-09-17 2007-09-27 2012-12-31
                      1
          2
                      2
## 13:
                              F 100
                                       alive 2009-04-09 2009-04-17 2012-12-31
## 14:
          2
                      3
                              F 103
                                       alive 2012-04-16 2012-04-20 2012-12-31
## 15:
          2
                      4
                              F 103
                                       alive 2012-04-24 2012-05-19 2012-12-31
          2
                      5
## 16:
                              F 103
                                       alive 2012-05-20 2012-05-25 2012-12-31
## 17:
          2
                      6
                              F 103
                                       alive 2012-08-19 2012-08-21 2012-12-31
```

So, these two patients are 'observed' 11 and 6 times through years, respectively.

These data format are very common when dealing with observational studies, or with chronic disease monitoring and with hospital admissions recording. In general, they are a well stabilized system to collect information.

1.2 Enhancing the Longitudinal Structure with augment()

Why the standard longitudinal structure is not enough if a multi-state model has to be run? A first observation could be that we are not able to infer anything about the state in which a given subject (i.e. patient) is at a particular point in time (i.e. hospital admission). The function augment() comes into play for this reason: to take advantage of the longitudinal structure in order to extract usable information to fuel a multi-state model. augment() takes a longitudinal dataset with exact starting and ending times and reshape it to produce an

augmented version. For instance, if you apply augment() to the dataset above, you get what follows:

```
hosp_augmented = augment( data = hosp, data_key = subj,
                            n events = adm number, pattern = label 2,
                            t start = dateIN, t end = dateOUT,
                            t cens = dateCENS, verbose = FALSE )
## Warning in augment(data = hosp, data_key = subj, n_events = adm_number, :
## no t_death has been passed. Assuming that dateCENS contains both censoring
## and death time
hosp_augmented[ 1:35, .( subj, adm_number, gender, age, label_2,
                           augmented, status, n status ) ]
##
       subj adm number gender age label 2 augmented status n status
##
    1:
           1
                       1
                              F
                                  83
                                        dead 2008-11-30
                                                               IN
                                                                      1 IN
    2:
           1
                       1
                              F
                                  83
##
                                         dead 2008-12-12
                                                              OUT
                                                                     1 OUT
    3:
           1
                       2
                              F
                                  83
                                         dead 2009-01-26
                                                               IN
##
                                                                      2 IN
                       2
    4:
                              F
                                  83
                                         dead 2009-02-16
                                                              OUT
##
           1
                                                                     2 OUT
##
    5:
           1
                       3
                              F
                                  83
                                        dead 2009-05-13
                                                               IN
                                                                      3 IN
    6:
           1
                       3
                              F
                                  83
                                         dead 2009-05-15
                                                              OUT
                                                                     3 OUT
##
##
    7:
           1
                       4
                              F
                                  83
                                         dead 2009-05-20
                                                               IN
                                                                      4 IN
    8:
                       4
                              F
                                  83
                                                              OUT
                                                                     4 OUT
##
           1
                                         dead 2009-05-25
   9:
                       5
                              F
                                  83
                                         dead 2009-06-12
##
           1
                                                               IN
                                                                      5 IN
## 10:
                       5
                              F
                                  83
                                         dead 2009-06-16
                                                                     5 OUT
           1
                                                              OUT
## 11:
                       6
                              F
                                  83
                                         dead 2009-06-20
                                                               IN
           1
                                                                      6 IN
                       6
## 12:
           1
                              F
                                  83
                                         dead 2009-06-25
                                                              OUT
                                                                     6 OUT
## 13:
                       7
                              F
                                  83
                                         dead 2009-07-17
                                                               IN
           1
                                                                      7 IN
## 14:
           1
                       7
                              F
                                  83
                                         dead 2009-07-22
                                                              OUT
                                                                     7 OUT
## 15:
           1
                       8
                              F
                                  84
                                         dead 2010-04-15
                                                               IN
                                                                      8 IN
## 16:
           1
                       8
                              F
                                  84
                                                              OUT
                                                                     8 OUT
                                        dead 2010-04-20
## 17:
                       9
           1
                              F
                                  84
                                         dead 2010-10-11
                                                               IN
                                                                      9 IN
## 18:
                       9
                              F
                                                              OUT
           1
                                  84
                                         dead 2010-10-14
                                                                     9 OUT
## 19:
                                  85
           1
                      10
                              F
                                        dead 2011-01-14
                                                               IN
                                                                     10 IN
## 20:
           1
                              F
                                                              OUT
                                                                    10 OUT
                      10
                                  85
                                         dead 2011-01-17
## 21:
           1
                      11
                              F
                                  85
                                         dead 2011-04-27
                                                               IN
                                                                     11 IN
## 22:
           1
                      11
                              F
                                  85
                                         dead 2011-04-28
                                                            DEAD
                                                                      DEAD
           2
## 23:
                       1
                              F
                                  99
                                        alive 2007-09-17
                                                               IN
                                                                      1 IN
           2
## 24:
                       1
                              F
                                  99
                                        alive 2007-09-27
                                                              OUT
                                                                     1 OUT
           2
                       2
## 25:
                              F 100
                                        alive 2009-04-09
                                                               IN
                                                                      2 IN
## 26:
           2
                       2
                                       alive 2009-04-17
                              F 100
                                                              OUT
                                                                     2 OUT
## 27:
           2
                       3
                              F 103
                                        alive 2012-04-16
                                                               IN
                                                                      3 IN
## 28:
           2
                       3
                              F 103
                                       alive 2012-04-20
                                                              OUT
                                                                     3 OUT
           2
                       4
## 29:
                              F 103
                                       alive 2012-04-24
                                                               IN
                                                                      4 IN
## 30:
           2
                       4
                              F 103
                                        alive 2012-05-19
                                                              OUT
                                                                     4 OUT
           2
## 31:
                              F 103
                                       alive 2012-05-20
                                                               IN
                                                                      5 IN
```

##	32:	2	5	F	103	alive	2012-05-25	OUT	5 OUT	
##	33:	2	6	F	103	alive	2012-08-19	IN	6 IN	
##	34:	2	6	F	103	alive	2012-08-21	OUT	6 OUT	
##	35:	2	6	F	103	alive	2012-08-21	OUT	6 OUT	
##		subj	${\tt adm_number}$	gender	age	label_2	augmented	status	n_status	

Despite the fact that not the same variables have been reported because of layout concerns, two things come up at first sight. In the first place, the number of rows is more than doubled. We now have 35 observations against the initial 17. In the second place, new variables have been created. We will describe them in a minute.

Given the complexity of the data, which can be very high, building a subject specific status flag which marks a its condition at given time steps, could be tricky and computationally intensive. At the end of the study, so at the censoring time, a subject, in general, can be alive, dead inside a given transition if death occurs within t_start and t_end , or outside a given transition if death occurs otherwise. After n events, the corresponding flag sequence is given by 2n + 1 for subjects alive and dead outside the transition, while it is just 2n for subjects who died inside of it. Let us consider an individual with 3 events. His/her status combinations will be as follows:

- ALIVE: IN-OUT | IN-OUT | IN-OUT | OUT
- **DEAD OUT**: IN-OUT | IN-OUT | IN-OUT | DEAD
- **DEAD IN**: IN-OUT | IN-OUT | IN-DEAD.

This operation produces a dataset in the augmented long format which allows to neatly model transitions between the given states.

From now on, we refer to each row as a transition for which we define a state in which the subject lies. augment() automatically creates 4 new variables (if argument more_status is missing):

- augmented: the new timing variable for the process when looking at transitions. If t_augmented is missing, then augment() creates augmented by default. augmented. The function looks directly to t_start and t_end to build it and thus it inherits their class. In particular, if t_start is a date format, then augment() computes a new variable cast as integer and names it augmented_int. If t_start is a difftime format, then augment() computes a new variable cast as a numeric and names it augmented_num;
- status: a status flag which looks at state. augment() automatically checks whether argument pattern has 2 or 3 unique values and computes the correct structure of a given subject. The variable is cast as character;
- status num: the corresponding integer version of status;
- *n_status*: a mix of *status* and *n_events* cast as character. *n_status* comes into play when a model on the progression of the process is intended.

1.2.1 Working correctly with augment()

The main and only aim of augment() is data wrangling. When dealing with complex structures as longitudinal data are, it is really important to introduce some rules which help the user to not fail when using the function. Here we discuss some of these rules which are mandatory in order to get a correct workflow with augment().

There are some arguments which are fundamental. They are pattern and state. pattern must contains the condition of a given subject at the end of the study. That is, how the subject is found at the censoring time. Because this peculiar structure is very common when dealing with hospital admission, the algorithm of augment() takes this framework as a reference. So, what does this mean? pattern can be either an integer, a factor or a character. Suppose we have it as an integer. augment() accepts only a pattern variable which have 2 or 3 unique values (i.e. running length(unique(pattern)) must return 2 or 3). Now, suppose we provide a variable with 3 unique values. They must be 0, 1, and 3, nothing different than that. The coding for this is as follows:

1. Case 1. integer:

- pattern = 0: subject is alive at the censoring time;
- pattern = 1: subject is dead during a transition;
- pattern = 2: subject is dead out of a transition.

2. Case 2. factor:

- pattern = 'alive': this is the first level of the factor and corresponds to pattern = 0 when integer;
- pattern = 'dead in': this is the second level of the factor and corresponds to pattern = 1 when integer;
- pattern = 'dead out': this is the third level of the factor and corresponds to pattern = 2 when integer;

3. Case 3. character:

• the unique values must be in alphabetical order to resemble the pattern of the integer and factor case.

In case one passes to pattern a variable which contains only two unique values, augment() automatically detects if the unit has an absorbing state occurred inside or outside a given transition. We suggest to always provide a variable with three unique values because of efficiency and speed.

Everything else different from what described above will inevitably produce wrong behaviour of augment() with and uncorrect results.

The second important argument is state. This is passed as a list and contains the status flags which will be used to compute all the status variables for the process. The length of state is 3, no less, no more and comes with a default given by: state = list('IN', 'OUT', 'DEAD'). The order is important here too. The status flags must be passed such that the first one ('IN') represents the first state (in hosp, being inside a hospital), the

second one represents the second state (in hosp, being outside a hospital), and the third one represents the absorbing state (in hosp, being dead inside or outside a hospital). As you can tell, this peculiar structure is typical of hospital admissions, where a patient can enter a hospital, can be discharged from it, or can die. As we have already see, the 'DEAD' status is reached no matter if the subject has died inside or outside a transition (i.e. in our case, inside or outside the hospital). One can change the flags in state, but they must be exactly 3. One may need a higher level of complexity when specifying the states of subjects. This will be discussed in the next section where state acts as the main indicator of states.

From version 1.2, augment() no longer checks the presence of missing data in the arguments passed to it. In fact, the new argument check_NA has been introduced and set to FALSE by default. Again, this is due because augment() has been developed just for restructuring data. The proceduring of searching for missing data is computationally intensive and could cause memory overheads. When dealing with very highly dimensional dataset, this becomes very unfeasible. We then suggest to perform all these types of checks before running augment(). If one really wants to run this procedure, can set check_NA = TRUE and detection will be performed over data_key, n_events, pattern, t_start and t_end. Beware, that no missing imputation or deletion is carried out. If any missing value is found, then augment() stops with error asking you to fix the problem.

1.3 What if a more complex status structure is needed?

augment() by default takes a very simple status structure given by 3 different values. In general, this is enough to define a multi-state model. But what if we need a more complex structure. Let's consider again the dataset hosp for the 3rd, 4th, 5th, and 6th patient with the following variables:

```
hosp[ 18:28, .( subj, adm number, rehab, it, rehab it,
                 dateIN, dateOUT, dateCENS ) ]
       subj adm number rehab it rehab it
##
                                                 dateIN
                                                           dateOUT
                                                                      dateCENS
##
    1:
          3
                       1
                                0
                                         df 2012-09-18 2012-09-27 2012-12-31
                             0
    2:
          3
                      2
                             0
                                1
                                         it 2012-11-28 2012-12-15 2012-12-31
##
                       3
##
    3:
          3
                             1
                                0
                                      rehab 2012-12-18 2012-12-28 2012-12-31
                       1
                                0
##
    4:
          4
                             0
                                         df 2008-08-13 2008-09-20 2012-12-31
                       2
                                0
##
    5:
          4
                             0
                                         df 2012-03-18 2012-03-19 2012-12-31
                       3
                                1
                                         it 2012-07-02 2012-07-20 2012-12-31
##
    6:
          4
                             0
                                         df 2006-02-09 2006-02-25 2008-04-16
##
    7:
          5
                       1
                             0
                                0
    8:
          6
                       1
                             0
                                0
                                         df 2009-03-05 2009-03-16 2010-12-19
##
##
    9:
          6
                       2
                             0
                                0
                                         df 2009-07-06 2009-07-20 2010-12-19
                                         df 2010-11-17 2010-11-23 2010-12-19
          6
                       3
## 10:
                             0
                                0
                       4
## 11:
          6
                             0
                                0
                                         df 2010-12-05 2010-12-19 2010-12-19
```

As you can see, we have two variables which take into account the type of hospital admission. rehab marks a rehabilitation admission while it marks an intensive therapy one. They are both binary and integer variables, so one can compose them to get something which is informative

and, at the same time, usable in the context of 'making a status'. We then created the variable $rehab_it$ which marks all the information in one place and it is a character. You can pass $rehab_it$ to the argument more_status to tell augment() to add these information into a new structure. Now, it is important to remember that augment() introduces some rules when you require to compute a more complex status structure. As you can see from the dataset, many values of $rehab_it$ are set to df. This stands for 'default' and when augment() finds it, it just compute the default status you already passed to argument state (i.e. in this case, it can be 'IN', 'OUT', or 'DEAD'). The argument more_status always looks for the value df, hence whenever you need to specify a default transition make sure to label it with this value. So, if we run augment() on this sample, we obtain the following:

```
hosp augmented_more = augment( data = hosp, data_key = subj,
                                  n events = adm number, pattern = label 2,
                                  t start = dateIN, t end = dateOUT,
                                  t_cens = dateCENS, more_status = rehab_it,
                                  verbose = FALSE )
## Warning in augment(data = hosp, data key = subj, n events = adm number, :
## no t death has been passed. Assuming that dateCENS contains both censoring
## and death time
hosp augmented more [ 36:60, . ( subj, adm number, rehab it,
                                  augmented, status, status exp, n status exp ) ]
        subj adm_number rehab_it
                                    augmented status status_exp n_status_exp
##
           3
##
    1:
                       1
                               df 2012-09-18
                                                   IN
                                                            df IN
                                                                        1 df IN
           3
                       1
                                                  OUT
##
    2:
                               df 2012-09-27
                                                           df OUT
                                                                       1 df OUT
                       2
           3
##
    3:
                                it 2012-11-28
                                                   IN
                                                            it_IN
                                                                        2 it IN
           3
                       2
                                                  OUT
                                                           it OUT
                                                                       2 it OUT
##
    4:
                                it 2012-12-15
##
    5:
           3
                       3
                            rehab 2012-12-18
                                                   ΙN
                                                         rehab_IN
                                                                     3 rehab_IN
                       3
##
    6:
           3
                            rehab 2012-12-28
                                                  OUT
                                                        rehab OUT
                                                                    3 rehab OUT
    7:
           3
                       3
##
                            rehab 2012-12-28
                                                  OUT
                                                        rehab OUT
                                                                    3 rehab OUT
##
    8:
           4
                       1
                               df 2008-08-13
                                                   IN
                                                            df_IN
                                                                        1 df_IN
                       1
                                                  OUT
                                                                       1 df_OUT
##
    9:
           4
                               df 2008-09-20
                                                           df OUT
                       2
## 10:
           4
                               df 2012-03-18
                                                   IN
                                                            df IN
                                                                        2 df IN
                       2
## 11:
           4
                               df 2012-03-19
                                                  OUT
                                                           df_OUT
                                                                       2 df OUT
                       3
## 12:
           4
                               it 2012-07-02
                                                   IN
                                                            it_IN
                                                                        3 it_IN
## 13:
           4
                       3
                                                  OUT
                                                                       3 it OUT
                                it 2012-07-20
                                                           it OUT
                       3
                                                  OUT
                                                           it_OUT
## 14:
           4
                                it 2012-07-20
                                                                       3 it_OUT
           5
                       1
                                                            df IN
                                                                        1 df IN
## 15:
                               df 2006-02-09
                                                   IN
## 16:
           5
                       1
                               df 2006-02-25
                                                  OUT
                                                           df_OUT
                                                                       1 df_OUT
## 17:
           5
                       1
                               df 2008-04-16
                                                 DEAD
                                                             DEAD
                                                                           DEAD
## 18:
           6
                       1
                                                            df IN
                                                                        1 df IN
                               df 2009-03-05
                                                   IN
## 19:
           6
                       1
                               df 2009-03-16
                                                  OUT
                                                           df_OUT
                                                                       1 df_OUT
                       2
## 20:
           6
                               df 2009-07-06
                                                   IN
                                                            df_IN
                                                                        2 df IN
           6
                       2
                                                  OUT
## 21:
                               df 2009-07-20
                                                           df OUT
                                                                       2 df OUT
                       3
           6
                                                            df_IN
                                                                        3 df IN
## 22:
                               df 2010-11-17
                                                   IN
```

```
## 23:
          6
                               df 2010-11-23
                                                 OUT
                                                         df OUT
                                                                     3 df OUT
                      3
## 24:
          6
                      4
                                                           df IN
                                                                      4 df IN
                               df 2010-12-05
                                                  IN
          6
## 25:
                               df 2010-12-19
                                                DEAD
                                                            DEAD
                                                                          DEAD
##
       subj adm number rehab it
                                   augmented status status exp n status exp
```

Beside the usual status variables, of which we reported only status, augment() computed two more:

- status_exp: is the direct expansion of status and the variable you passed to more_status, which in this case is rehab_it. The function composes them by pasting a '_' in between. This is the main reason why it is worth to build a character variable if you know you need to fuel it in as an indicator of a more complex status structure;
- status_exp_num: the corresponding integer version of status_exp;
- n_status_exp: similar to what has been done before, augment() mixes information coming from the current expandend status and the number of admission to give you the time evolution of the process.

2 Graphical Assessment of a Multi-state Model

msmtools has been mainly developed to easily manage and work with longitudinal datasets which need to be restructured in order to get msm to work properly.

However, msmtools comes with two more functions which try to address graphically and in a very efficient way the problem of the Goodness-of-Fit (GoF) for a multi-state model. When dealing with this type of models, GoF is always a tough quest. Furthermore, up to now, no formal statistical tests are defined when a multi-state model is computed within an exact time framework (Titman and Sharples 2009) (Titman and Sharples 2008).

2.1 Comparing fitted and empirical survival with survplot()

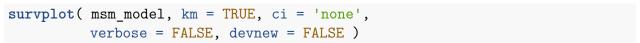
One of the most common graphical method to assess whether a multi-state model is behaving the way we expect, is to compare the empirical survival with the fitted one. survplot() helps out doing this and few more things. The function is a wrapper of the already known plot.survfit.msm() from the package msm.

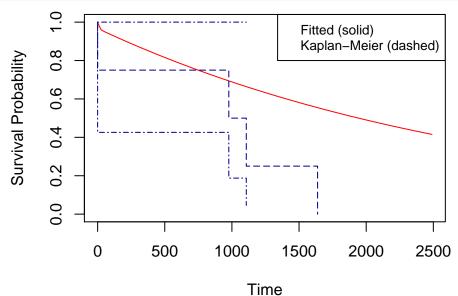
Suppose we ran a multi-state model on dataset hosp with the following code:

```
# let's define the initial transition matrix for our model
Qmat = matrix( data = 0, nrow = 3, ncol = 3, byrow = TRUE )
Qmat[ 1, 1:3 ] = 1
Qmat[ 2, 1:3 ] = 1
colnames( Qmat ) = c( 'IN', 'OUT', 'DEAD' )
rownames( Qmat ) = c( 'IN', 'OUT', 'DEAD' )
Qmat
```

```
##
        IN OUT DEAD
## IN
         1
             1
                  1
## OUT
         1
             1
                  1
## DEAD
         0
             0
                  0
# attaching the msm package and running the model using
# gender and age as covariates
library( msm )
msm model = msm( status_num ~ augmented_int,
                 subject = subj, data = hosp augmented,
                 covariates = ~ gender + age,
                 exacttimes = TRUE, gen.inits = TRUE,
                 qmatrix = Qmat, method = 'BFGS',
                 control = list( fnscale = 6e+05, trace = 0,
                                  REPORT = 1, maxit = 10000)
```

We now have a multi-state model for which we can carry out some graphical inspections. So, we want a simple comparison between the fitted survival curve and the empirical one, computed using the Kaplan-Meier estimator. The code is as follows:

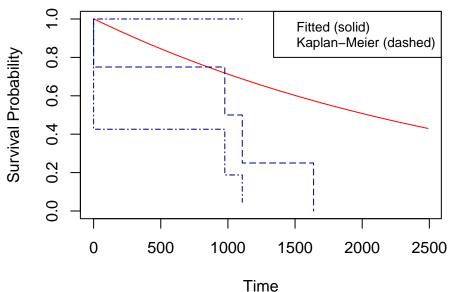




With no surprises, the plot is not so satisfying due to the really small dataset we provided.

Now, survplot() takes several parameters, many of them come with a default value. For instance, the figureabove has been computed for a transition (IN - DEAD). We can pass to argument from any starting state we want. If to is missing, survplot() will check what is the higher value in the corresponding msm object and grabs it. Of course, you are free to compute any survival you want, given the transition is allowed in the initial transition matrix

Qmat. Let's plot the survival comparison for the transition (OUT - DEAD):

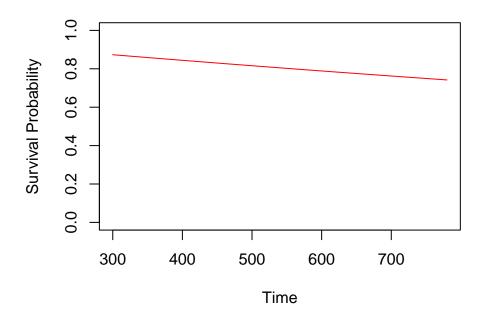


If we do not want to show the Kaplan-Meier, we can pass km = FALSE, which is the default.

2.1.1 Defining a custom time sequence

By default survplot() computes the fitted survival on a given grid. The number of grid points is given by grid. In some cases, one would like to pass a custom time sequence. This can be achieved by passing the argument times a numeric vector. Now grid is ignored.

Consider our dataset and suppose we want to compute a fitted survival only fo specific points in time. The following code addresses this request.



2.1.2 Obtaining the dataset for the Kaplan-Meier

It is possible to tell survplot() to return the associated Kaplan-Meier dataset by setting return.km = TRUE. This fastly computes the data through data.table. Passing only km = TRUE won't return any data, even if they must be computed anyway to plot results.

No results are printed. If you want to store the information in the current environment, you must assign survplot() to an object as follows:

```
# running survplot() and assigning it to an object
km_data = survplot( msm_model, ci = 'none', return.km = TRUE,
                     verbose = FALSE, do.plot = FALSE )
# let's see the dataset
head( km_data )
##
      subject mintime mintime exact anystate
## 1:
             1
                                 1107
                                              1
                 15092
## 2:
            5
                 13985
                                    0
                                              1
## 3:
            6
                 14962
                                  977
                                              1
            7
## 4:
                 15623
                                 1638
                                              1
```

The structure of the data is consistent. survplot() always computes a dataset in wide format, as requested by survfit with 3 columns:

- *subject*: the ordered subject ID as passed to msm function;
- *mintime*: the time at which the event occurred;
- anystate: tansition indicator to compute the Kaplan-Meier.

The only modification you might encounter really depends on argument exacttimes. This is inherited from msm function whose aim was to tell the model that transitions occurred at exact and known times, including deaths. This is the main reason why this argument should always be set the same way you set it in msm. In our case, we do have a multi-state model in which transitions are well known and exact as you can see from the msm call above. survplot() puts exacttimes = TRUE by default so we don't have to worry about it. So, when exacttimes = TRUE, survplot() adds a new time variable which provides the relative time for each transition within a given subject. For instance, km_data has another column named mintime_exact which is cast the same way of augmented.

2.1.3 Obtaining the dataset for the fitted survival

Similarly to what done for the Kaplan-Meier, it is possible to obtain the data used to compute the fitted survival as well. This can be achieve by setting return.p = TRUE. If times is passed, then the resulting dataset will have as many rows as the elements in times. If times is missing, then survplot() uses grid to know how many time points are requested. Below there is the snippet that addresses what described.

As before, saving the data in the current environment follows the same procedure as seen before:

```
# running survplot() and assigning it to an object
fitted data = survplot( msm model, ci = 'none', grid = 10, return.p = TRUE,
                        verbose = FALSE, do.plot = FALSE )
# let's see the dataset
fitted_data
##
         time probs
##
   1:
          1.0 0.9957
##
    2:
        252.4 0.8875
##
   3:
       503.8 0.8149
        755.2 0.7483
##
   4:
##
    5: 1006.6 0.6871
   6: 1258.0 0.6309
##
   7: 1509.4 0.5793
##
   8: 1760.8 0.5319
##
   9: 2012.2 0.4884
## 10: 2263.6 0.4485
```

The structure of the data is consistent here too. **survplot()** always computes a dataset in wide format with 2 columns:

• time: time at which to compute the fitted survival. It can be obtained either by grid

or by times so that the cardinality of the data depends on them;

• probs: the corresponding value of the fitted survival.

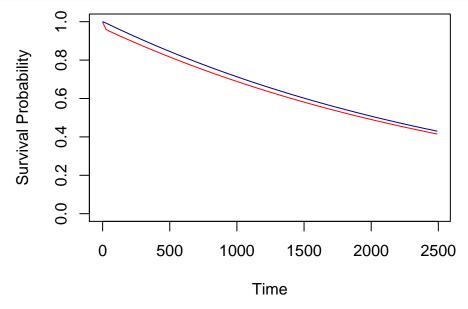
Of course, you can request survplot() to return both the datasets by passing all the parameters. Below you can see the code and the output when no assignment is done and when you save the data into a new object.

all_data is a list of two elements. If you want to split up the datasets, just use common syntax:

```
# do not extract data using just one [].
# This keeps the class, so it returns a list
km data wrong = all data[ 1 ]
# extracting data using the list way so be careful to use double []
km_data_1 = all_data[[ 1 ]]
# extracting data using the '$' access operator
km data 2 = all data$km
identical( km_data_wrong, km_data_1 )
## [1] TRUE
identical( km data 1, km data 2 )
## [1] TRUE
km data 1
## NULL
fitted data 1 = all data[[ 2 ]]
fitted data 2 = all data$fitted
identical( fitted data 1, fitted data 2 )
## [1] TRUE
fitted_data_1
## NULL
```

2.1.4 The plot layering

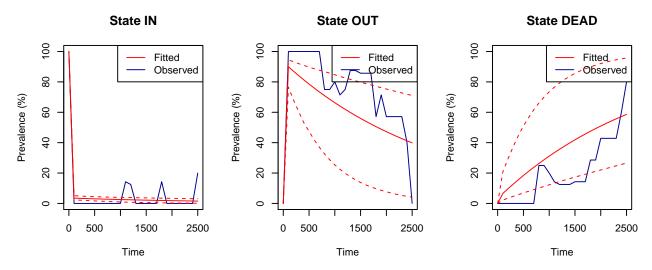
Multi-state models, as their name suggests, are specifically designed to work when more than one status exists. Infact, they tipically work when more than 2 status are present. In our example, we have 3 states: 'IN, 'OUT', 'DEAD. Now, what if we want to plot on the same device more than just one fitted survival curve? Suppose we want to plot the expected survival computed from state 1 and 2. That means, from 'IN and 'OUT' to 'DEAD'. The plot layering addresses exactly this problem and survplot() supports this with the argument add. Let's see this in the following example:



2.2 Comparing expected and observed prevalences with prevplot()

A second graphical tool which helps us in the attempt to understand the goodness of the model is given by comparing the expected and observed prevalences. prevplot() is a wrapper of the plot.prevalence.msm() function inside the msm package but, again, it does more things.

Consider the multi-state model we have built above. We can compute the prevalences using prevalence.msm() function. This produces a named list which will be used inside prevplot(). For instance, running the following code produces a plot of prevalences for each state of the model.

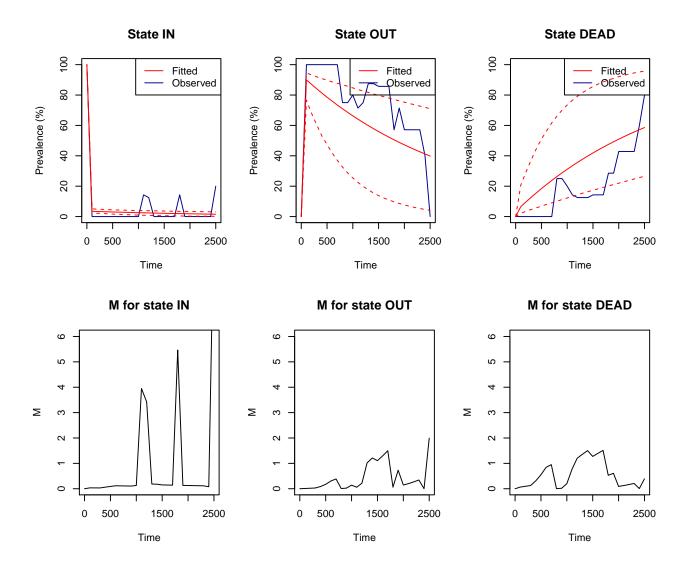


It is mandatory for prevplot() to work with a msm object and a list compute by prevalence.msm are passed.

It is also possibile to plot the following statistic:

$$M = \frac{(O_{is} - E_{is})^2}{E_{is}}$$

which gives an idea of the deviance from the Markov model. This is computed according to Titman and Sharples (2008). The following code addresses this request.



2.3 A note on verbose and devnew

We are not going to discuss every arguments inside every function. This paragraph serves as a guideline to better exploit msmtools. We have developed the package by paying lot of attention to the consistency of the code throughout the functions.

For example, you can find the argument verbose anywhere in the package. This is useful when you do not want to be informed about anything that is happening internally with the only exception for warnings and of course errors. If quiet is your mood, then you may want to set verbose = FALSE.

A second argument which is shared between survplot() and prevplot() is devnew. This is a purely graphical parameter which is set to TRUE by default. It allows you to decide whether to plot on a new graphical device called with dev.new() by default. If you set devnew = FALSE, then the plot is overwritten according to dev.cur(). There exist two caveat: the former is that devnew is bypassed if the argument add = TRUE is passed to survplot(). This means that, when you want to add a new layer to an existing plot (with add), it does

not make any sense to let the function using a new device. Hence, devnew is simply ignored. The latter is that, even you can set devnew = FALSE in prevplot(), one should keep it as the default. If you set it to FALSE and you want to plot M by setting M = TRUE, then this plot overwrites the prevalence one.

Dowle, M., T. Short, S. Lianoglou, A. Srinivasan with contributions from R. Saporta, and E. Antonyan. 2014. data.table: Extension of data.frame. http://CRAN.R-project.org/package=data.table.

Jackson, C. H. 2011. "Multi-State Models for Panel Data: The msm Package for R." *Journal of Statistical Software* 38 (8): 1–29.

Titman, Andrew C, and Linda D Sharples. 2008. "A General Goodness-of-Fit Test for Markov and Hidden Markov Models." *Statistics in Medicine* 27 (12). Wiley Online Library: 2177–95.

——. 2009. "Model Diagnostics for Multi-State Models." Statistical Methods in Medical Research. SAGE Publications.