

Adverse Events

AE Parameterization

Define an Adverse Event

Usage:

```
AE(  
  time_to_first_event,  
  event_duration,  
  time_between_events,  
  severity_probability = c(1/3, 1/3, 1/3)  
)
```

Arguments:

time_to_first_event: Expected time until the first event (in days)

event_duration: Expected duration of each event (in days)

time_between_events: Expected time between events (in days)

severity_probability: Probability distribution for event severity (vector of probabilities)

Probability of severeties:

##		1	2	3
## equal	0.3333333	0.3333333	0.3333333	
## low	0.8000000	0.1500000	0.0500000	
## medium	0.1500000	0.8000000	0.0500000	
## high	0.0500000	0.1500000	0.8000000	

Define an Adverse Events

```
simulate_events(AEs, max_time, n_it = 100)
```

Arguments

AEs: AE or a list of AE objects max_time: Maximum time to simulate events (in days)

Examples

Increasing Time to first event

```
par(mfrow = c(2, 2))

event <- AE(time_to_first_event = 10, event_duration = 5, time_between_events = 25, severity_probabilit
simulated_events<- simulate_events(list(event),max_time=180,n_it = 10000)
h<-score_distribution(scores(simulated_events),main=NULL,
                      sub=str(event))

### increasing the time to the first event
event <- AE(time_to_first_event = 100, event_duration = 5, time_between_events = 25, severity_probabil

simulated_events<- simulate_events(list(event),max_time=180,n_it = 10000)

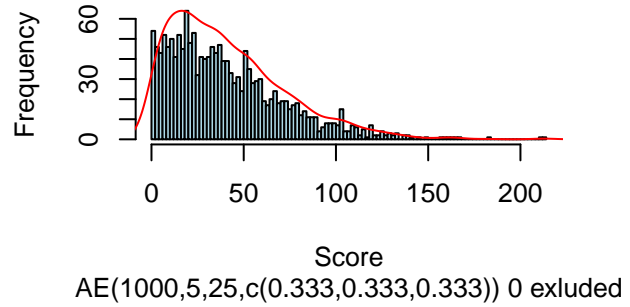
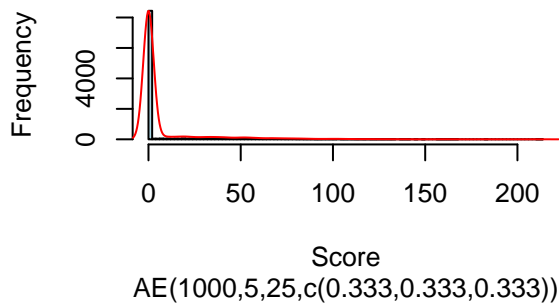
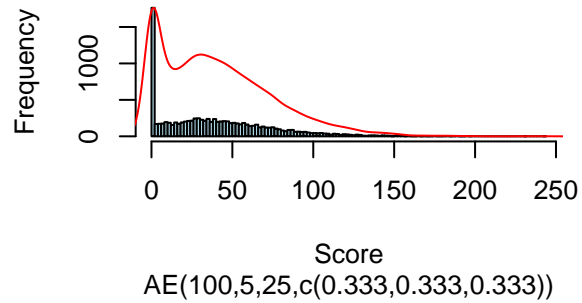
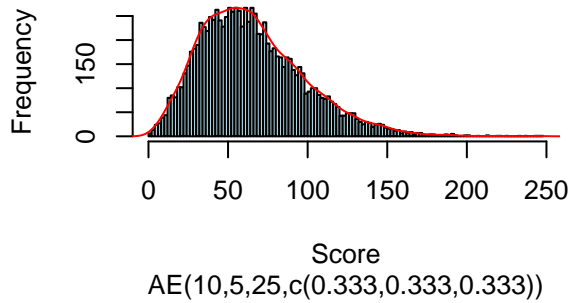
h<-score_distribution(scores(simulated_events),main=NULL,
                      sub=str(event))

### increasing the time to the first event excluding 0
event <- AE(time_to_first_event = 1000, event_duration = 5, time_between_events = 25,
            severity_probability = SEVERITY_PROBABILITIES$equal)

simulated_events<- simulate_events(list(event),max_time=180,n_it = 10000)

h<-score_distribution(scores(simulated_events),main=NULL,sub=str(event))

### increasing the time to the first event excluding 0
h<-score_distribution(scores(simulated_events),exclude_zero=TRUE,main=NULL,
                      sub=paste0(str(event)," 0 exluded"))
```



Increasing the event duration

```
source("R/event_analysis.R")

par(mfrow = c(1,1))
ymax=4300
c1 <- rgb(255,116,30,max = 255, alpha = 60)
c2 <- rgb(144, 238, 144, max = 255, alpha = 60)
c3 <- rgb(173, 216, 230, max = 255, alpha = 60)
n_it <- 10000

event <- AE(time_to_first_event = 20, event_duration = 100, time_between_events = 25, severity_probabil
simulated_events.high_duration<- simulate_events(list(event),max_time=180,n_it = n_it)
h3 <- score_distribution(scores(simulated_events.high_duration),col=c1,ymax=ymax)

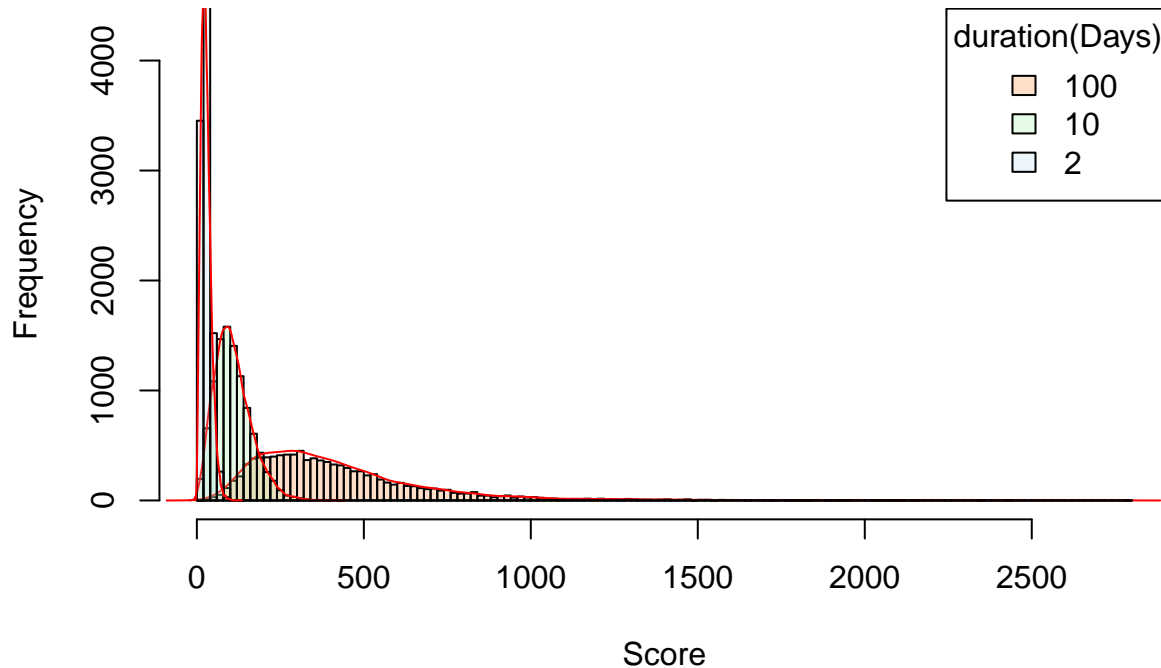
event <- AE(time_to_first_event = 20, event_duration = 10, time_between_events = 25, severity_probabili
simulated_events.medium_duration<- simulate_events(list(event),max_time=180,n_it = n_it)

h2 <- score_distribution(scores(simulated_events.medium_duration),add=TRUE,col = c2,breaks=h3$breaks)

event <- AE(time_to_first_event = 20, event_duration = 2, time_between_events = 25, severity_probabilit
simulated_events.small_duration<- simulate_events(list(event),max_time=180,n_it = n_it)

h1 <- score_distribution(scores(simulated_events.small_duration),col = c3,add=TRUE,breaks=h3$breaks)
```

```
legend("topright", title = "duration(Days)", legend = c("100", "10", "2"), fill = c(c1, c2, c3))
```



Increasing the time between adverse events

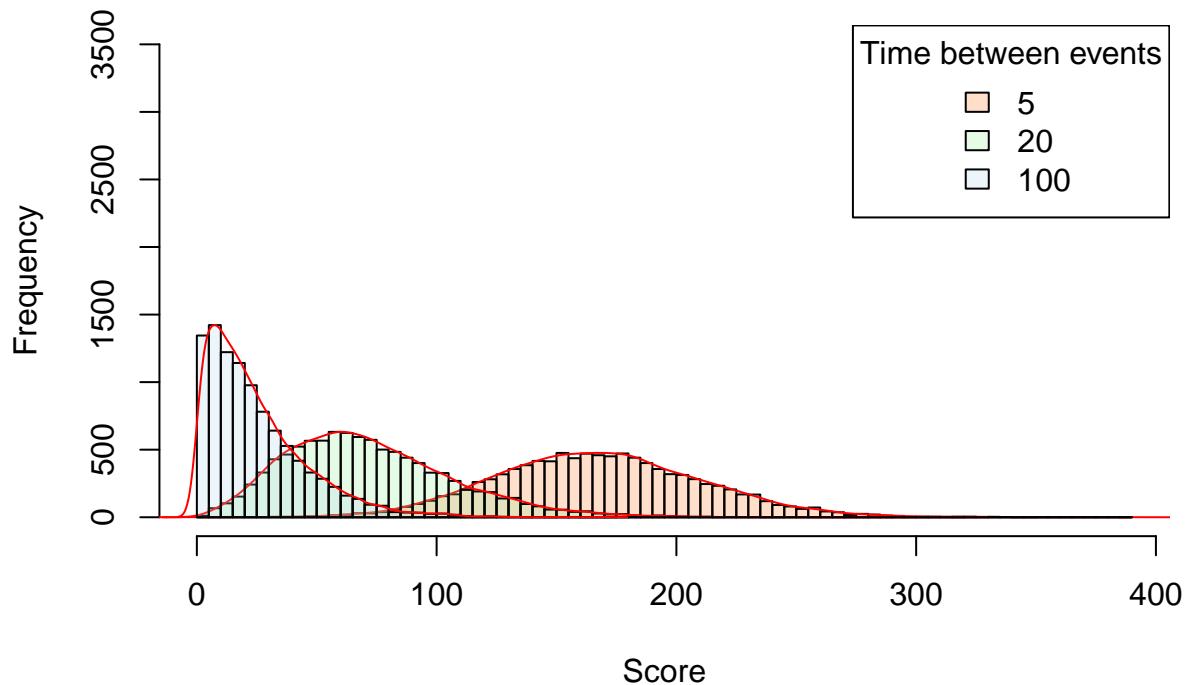
```
par(mfrow = c(1,1))
ymax=3500

event <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 5, severity_probability = 0.5)
simulated_events<- simulate_events(list(event),max_time=180,n_it = n_it)
h1<-score_distribution(scores(simulated_events),col=c1,ymax=ymax)

### Doubling the event duration
event <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 20, severity_probability = 0.5)
simulated_events<- simulate_events(list(event),max_time=180,n_it = n_it)
h2<-score_distribution(scores(simulated_events),col=c2,add=TRUE,breaks=h1$breaks)

### increasing the event duration
event <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 100, severity_probability = 0.5)
simulated_events<- simulate_events(list(event),max_time=180,n_it = n_it)
h2<-score_distribution(scores(simulated_events),col=c3,add=TRUE,breaks=h1$breaks)

legend("topright", legend = c(5,20,100), fill = c(c1,c2,c3), title = "Time between events")
```



With a larger time between events there is mostly only one event

Different severity probabilities

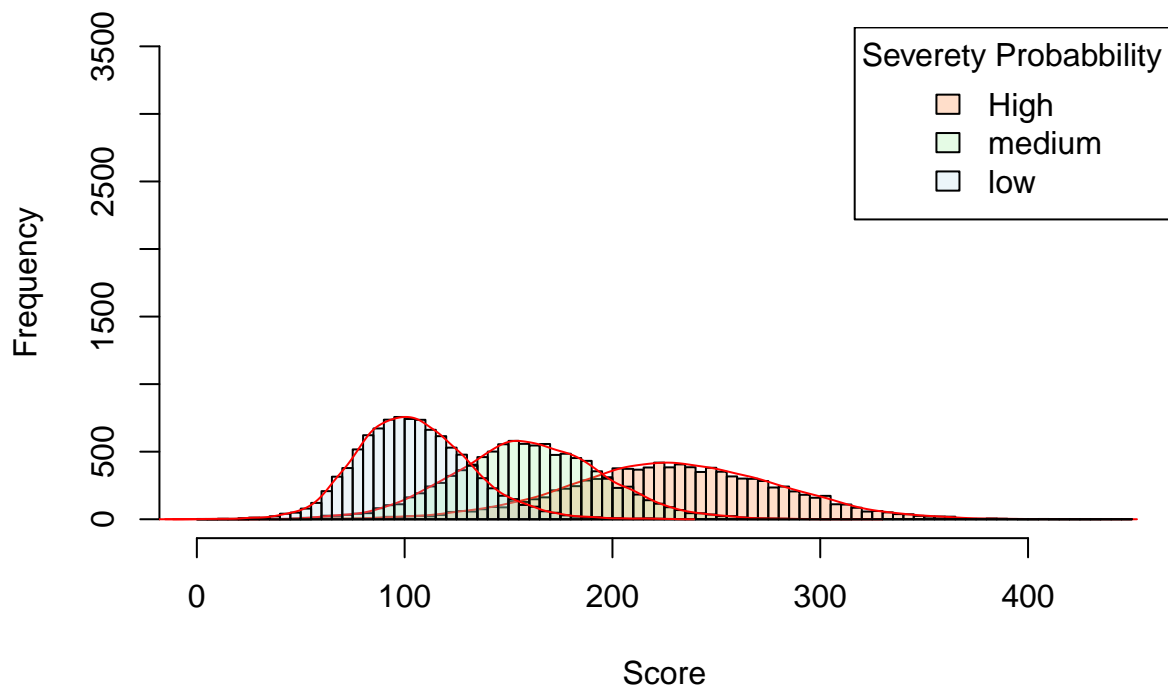
```
par(mfrow = c(1,1))
ymax=3500
breaks <- seq(0,450,5)

event <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 5, severity_probability)
simulated_events<- simulate_events(list(event),max_time=180,n_it = n_it)
h1 <-score_distribution(scores(simulated_events),col=c1,ymax=ymax,breaks=breaks)

event <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 5, severity_probability)
simulated_events<- simulate_events(list(event),max_time=180,n_it = n_it)
h2<-score_distribution(scores(simulated_events),col=c2,add=TRUE,breaks=breaks)

### increasing the event duration
event <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 5, severity_probability)
simulated_events<- simulate_events(list(event),max_time=180,n_it = n_it)
h3<-score_distribution(scores(simulated_events),col=c3,add=TRUE,breaks=breaks)

legend("topright", legend = c("High","medium","low"), fill = c(c1,c2,c3), title = "Severity Probabbility")
```



Shifts the distribution

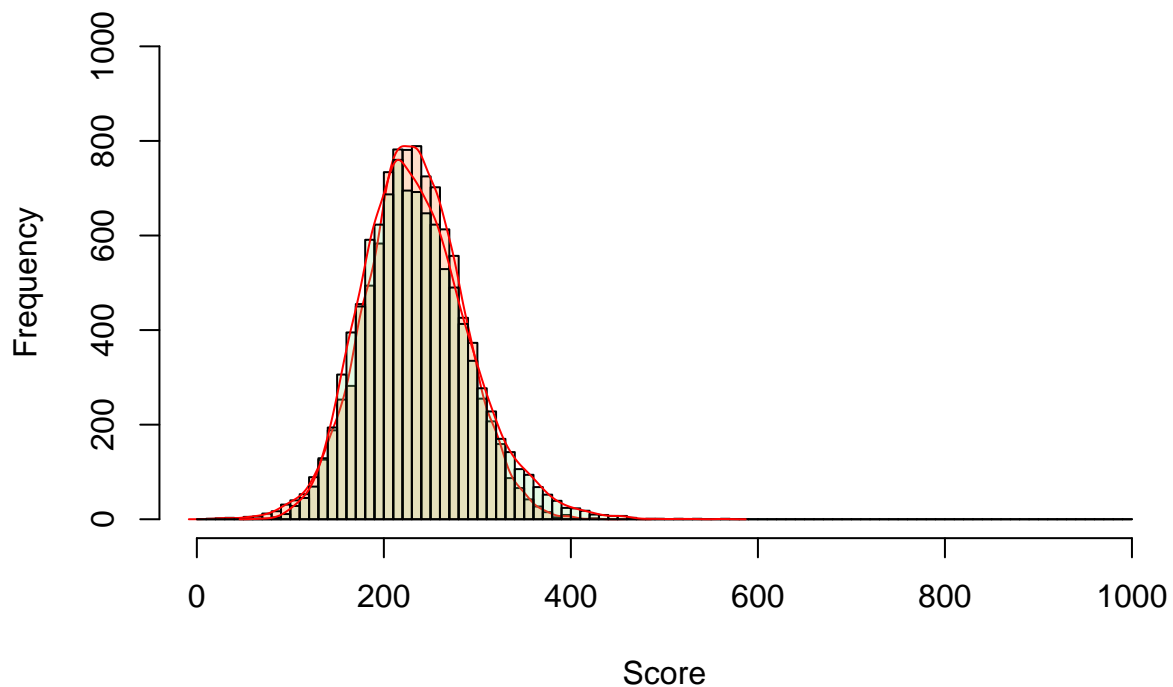
Achieving similar distributions

The distributions of AE(20,5,5,high) resembles the one from AE(0,10,6.3,high)

```
n_it = 10000
breaks = seq(0,1000,10)
ymax = 1000

event <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 5, severity_probabilities = c(0.5, 0.3, 0.2))
simulated_events <- simulate_events(list(event), max_time=180, n_it = n_it)
h1 <- score_distribution(scores(simulated_events), col=c1, ymax=ymax, breaks=breaks)

event <- AE(time_to_first_event = 0, event_duration = 10, time_between_events = 6.3, severity_probabilities = c(0.5, 0.3, 0.2))
simulated_events <- simulate_events(list(event), max_time=180, n_it = n_it)
h1 <- score_distribution(scores(simulated_events), col=c2, add=TRUE, breaks=breaks)
```



Combining events

```
par(mfrow = c(2,1))

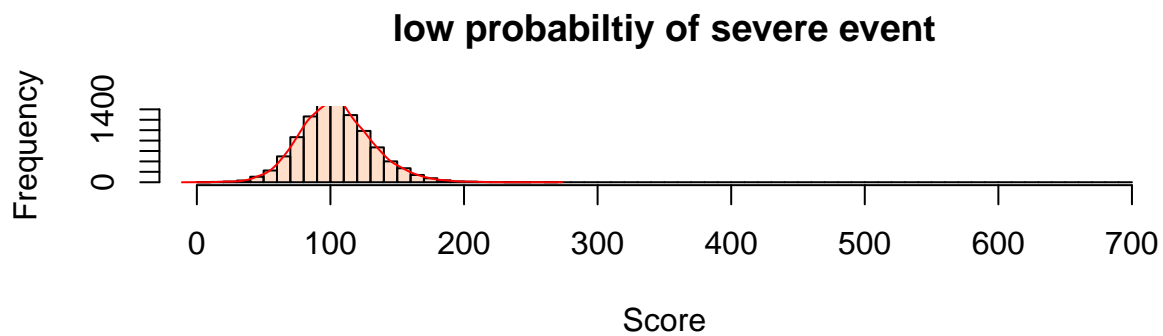
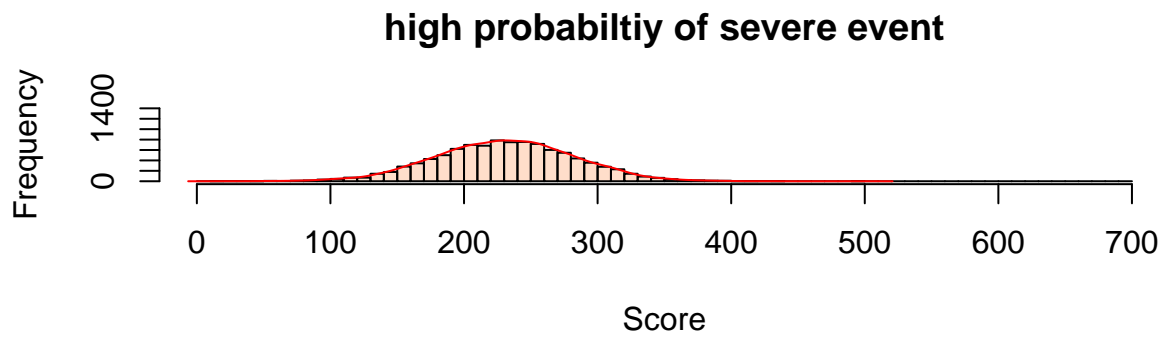
breaks = seq(0,700,10)
ymax = 1400

event.high <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 5, severity_probabi
event.low <- AE(time_to_first_event = 20, event_duration = 5, time_between_events = 5, severity_probabi

simulated_events.high<- simulate_events(list(event.high),max_time=180,n_it = n_it)

h1 <-score_distribution(scores(simulated_events.high),col=c1,ymax=ymax,breaks=breaks,
main="high probabiltiy of severe event")

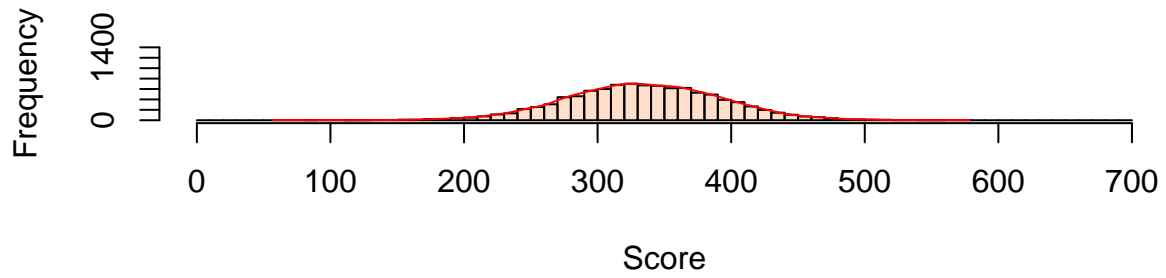
simulated_events.low<- simulate_events(list(event.low),max_time=180,n_it = n_it)
h1 <-score_distribution(scores(simulated_events.low),col=c1,ymax=ymax,breaks=breaks,
main="low probabiltiy of severe event")
```



```
## scores together
simulated_events<- simulate_events(list(event.low,event.high),max_time=180,n_it = n_it)
par(mfrow = c(2,1))
h1 <-score_distribution(scores(simulated_events),col=c1,ymax=ymax,breaks=breaks,
                        main= "scores of the two events together")

h<-score_distribution(scores(simulated_events.high)+scores(simulated_events.low),col=c1,ymax=ymax,breaks=breaks)
```


scores of the two events together



scores added afterwards

