Tutorials and worked examples for simulation, curve fitting, statistical analysis, and plotting.
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The Mantel-Haenszel test and related procedures are used to compare two sets of survival data and to test for the suitability of the exponential, Weibull, Gompertz, Cox, and extreme value survival models.

From the main SIMFIT menu choose [Statistics], [Time series and survival], then [Kaplan-Meier] for two samples, and study the default test files `survive.tf3` and `survive.tf4` with data for remission from Leukemia from Frierich et al, Blood, 21, 699-716, 1963 in the following formats.

`survive.tf3`: 6-MP data

Time	Code	Number
6	0	3
6	1	1
7	0	1
9	1	1
10	0	1
10	1	1
11	1	1
13	0	1
16	0	1
17	1	1
19	1	1
20	1	1
22	0	1
23	0	1
25	1	1
32	1	2
34	1	1
35	1	1

`survive.tf4`: Placebo data

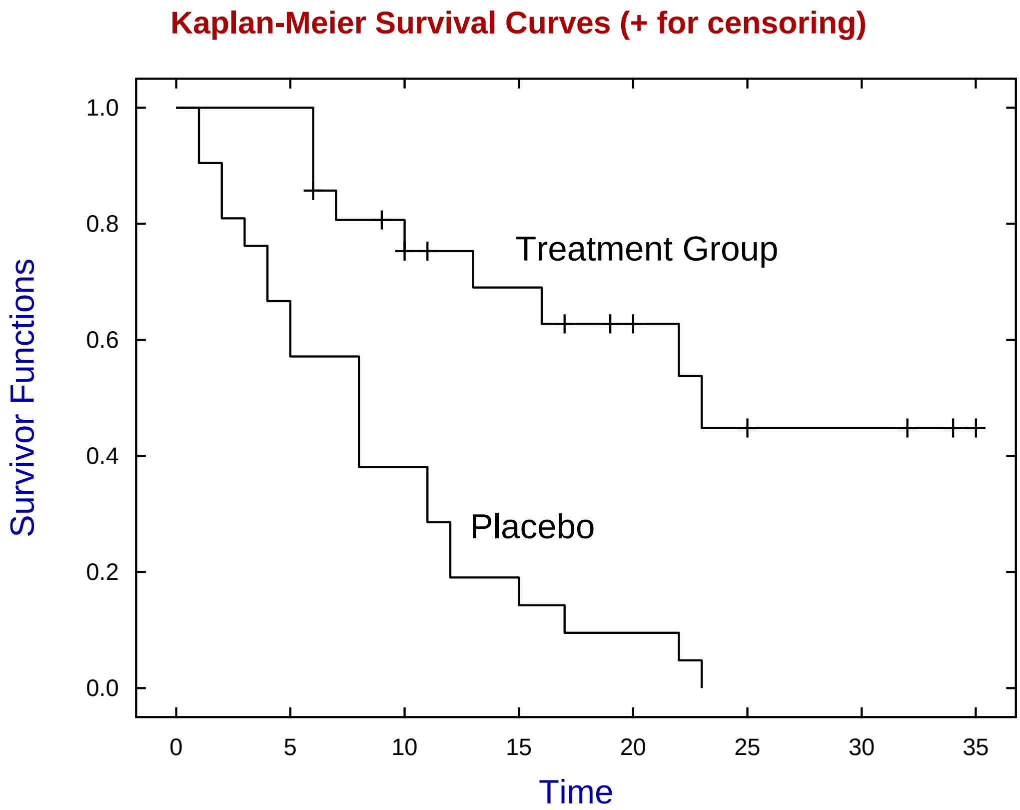
1	0	2
2	0	2
3	0	1
4	0	2
5	0	2
8	0	4
11	0	2
12	0	2
15	0	1
17	0	1
22	0	1
23	0	1

- Column 1: time (not necessarily ordered)
- Column 2: censoring code (0 = failure, 1 = right-censored)
- Column 3: frequency of the observation
  Note: The starting sample size will be taken as the sum of all the frequencies in column 3. So subjects remaining at or after the last failure should be included as right-censored with the appropriate frequency.

The results from the Mantel-Haenszel log-rank test are recorded in the next table.

For `survive.tf3`: 9 failures, 12 censored		
For `survive.tf4`: 21 failures, 0 censored		
$H_0 : h_A(t) = h_B(t)$ (equal hazards)		
$H_1 : h_A(t) = \theta h_B(t)$ (proportional hazards)		
QMH test statistic	16.79	
$P(\chi^2 \geq QMH)$	0.0000	*Reject H_0 at 1% significance level*
Estimate for θ	0.1915	
95% confidence range	0.0828, 0.4429	

The conclusion that the two groups differ significantly is reinforced by the next figure showing the Kaplan-Meier survivor functions, including censored data, from this analysis.



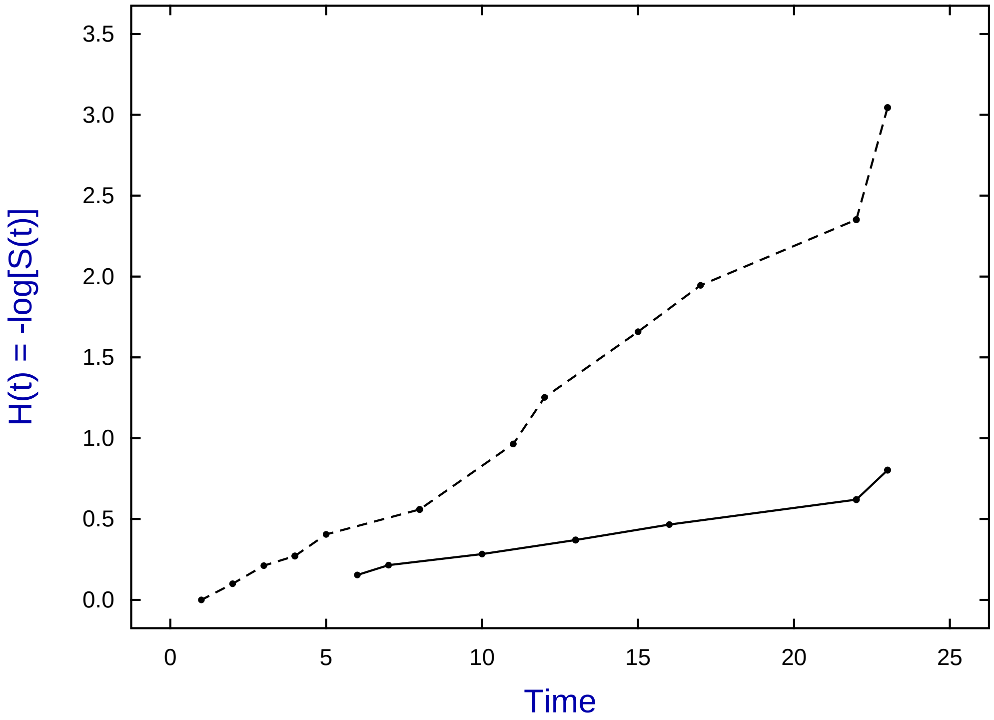
Also, various graphs can be plotted to explore the form of the estimated hazard function $\hat{h}(t)$ and estimated cumulative hazard function $\hat{H}(t)$ for the commonly used models based on the identities

$$\begin{aligned} \text{Exponential} &: H(t) = At \\ \text{Weibull} &: \log(H(t)) = \log A^B + B \log t \\ \text{Gompertz} &: \log(h(t)) = \log B + At \\ \text{Extreme value} &: \log(H(t)) = \alpha(t - \beta). \end{aligned}$$

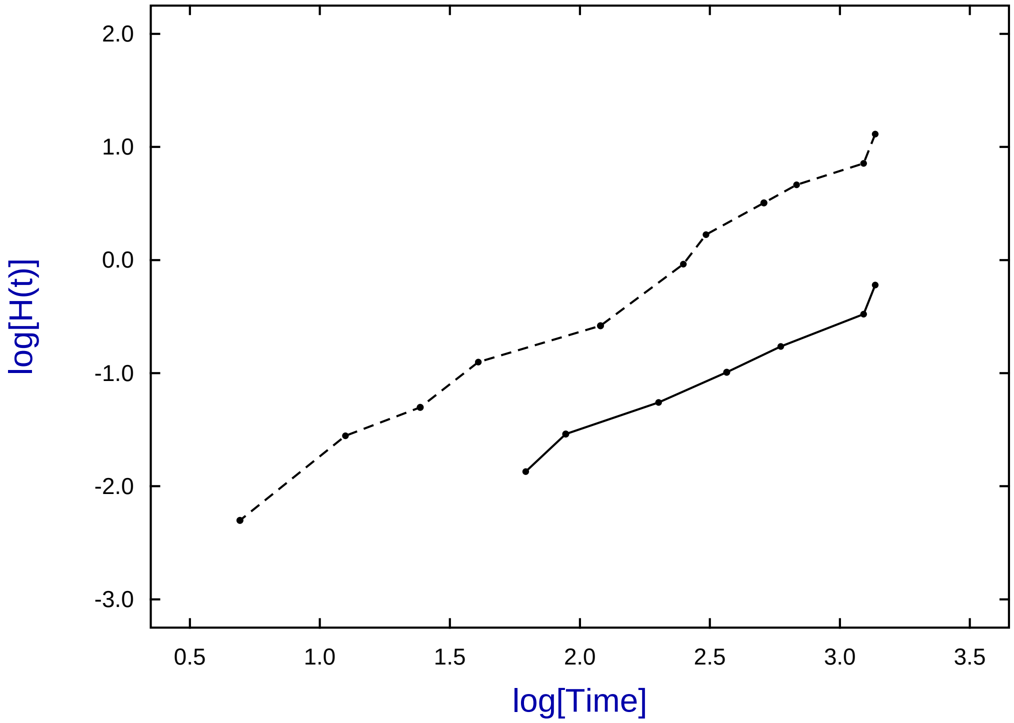
For instance, $\hat{H}(t)$ would be linear for the exponential model, for the Weibull distribution a plot of $\log(-\log(\hat{S}(t))$ against $\log t$ should be linear, while the proportional hazards assumption would merely alter the constant term since, for $h(t) = \theta AB(At)^{B-1}$,

$$\log(-\log(S(t)) = \log\theta + \log A^B + B \log t.$$

Checking the Exponential Survival Model



Checking the Weibull Survival Model



Theory

To understand the graphical and statistical tests used to compare two samples, and to appreciate the results displayed in the previous results table, consider the relationship between the cumulative hazard function $H(t)$ and the hazard function $h(t)$ defined as follows

$$\begin{aligned} h(t) &= f(t)/S(t) \\ H(t) &= \int_0^t h(u)\,du \\ &= -\log(S(t)). \end{aligned}$$

Testing for the presence of a constant of proportionality in the proportional hazards assumption amounts to testing the value of θ with respect to unity. If the confidence limits in the results table enclose 1, this can be taken as suggesting equality of the two hazard functions, and hence equality of the two distributions, since equal hazards implies equal distributions.

The QMH statistic given in the results table can be used in a chi-square test with one degree of freedom for equality of distributions, and it arises by considering the 2 by 2 contingency tables at each distinct time point t_j of the following type.

	Died	Survived	Total
Group A	d_{jA}	$n_{jA} - d_{jA}$	n_{jA}
Group B	d_{jB}	$n_{jB} - d_{jB}$	n_{jB}
Total	d_j	$n_j - d_j$	n_j

Here the total number at risk n_j at time t_j also includes subjects subsequently censored, while the numbers d_{jA} and d_{jB} actually dying can be used to estimate expectations and variances such as

$$\begin{aligned} E(d_{jA}) &= n_{jA} d_j / n_j \\ V(d_{jA}) &= \frac{d_j(n_j - d_j) n_{jA} n_{jB}}{n_j^2(n_j - 1)}. \end{aligned}$$

Now, using the sums

$$\begin{aligned} O_A &= \sum d_{jA} \\ E_A &= \sum E(d_{jA}) \\ V_A &= \sum V(d_{jA}) \end{aligned}$$

as in the Mantel-Haenszel test, the log rank statistic can be calculated as

$$QMH = \frac{(O_A - E_A)^2}{V_A}.$$

Clearly, the graphs, the value of θ with 95% confidence range not enclosing 1, and the chi-square test with one degree of freedom all support the hypothesis that the the assumption of a Weibull distribution with proportional hazards but not equal hazards cannot be rejected with these data.