

Bayesian Statistics

Time-to-Event Models

Brani Vidakovic, Ph.D.

Professor

School of Industrial and Systems Engineering



GTx

Before We Begin...

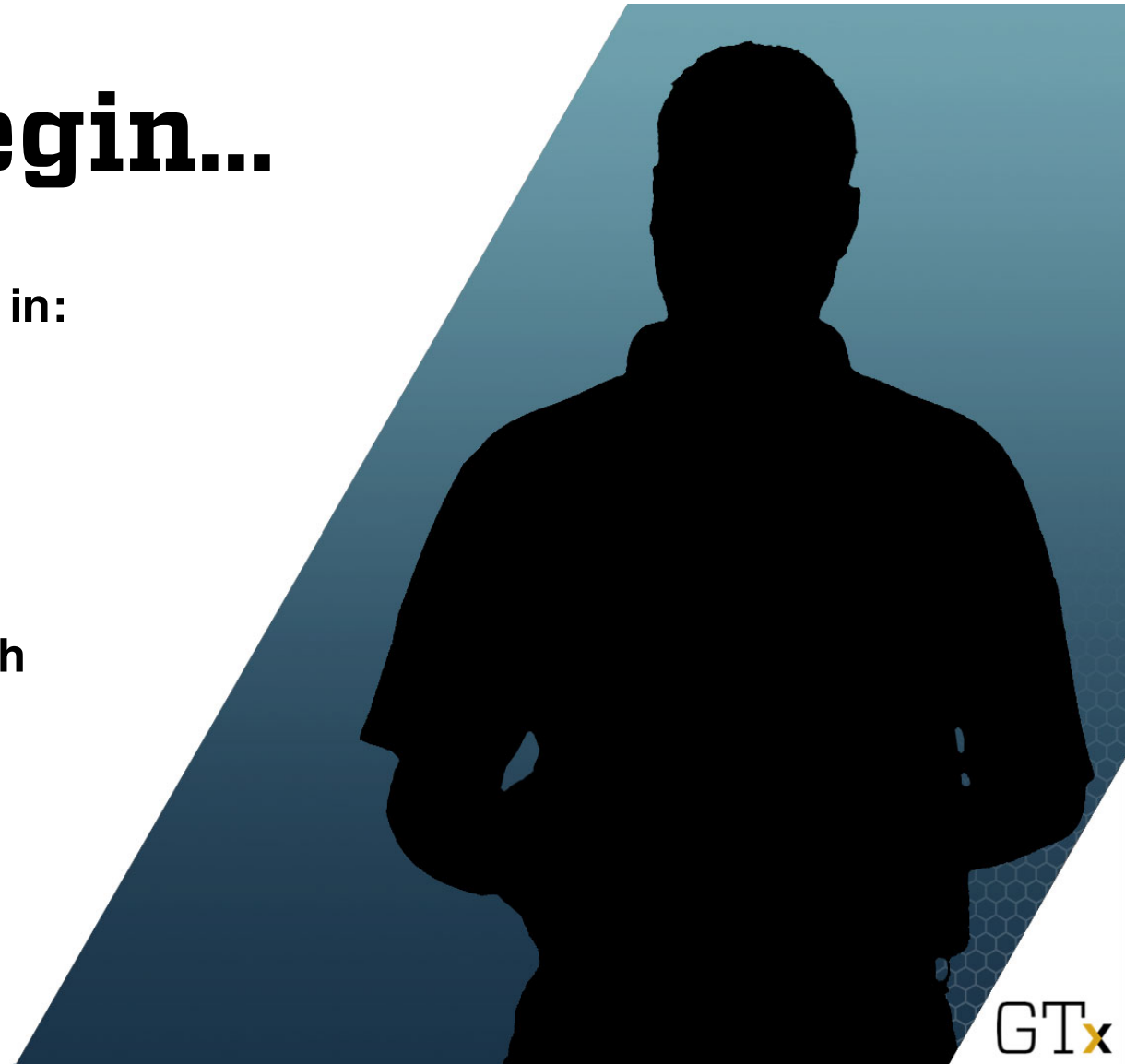
Time-to-Event models applied in:

Reliability Theory

Survival Theory

Geoscientific Prediction

Focus on Parametric Approach




Lifetime Distributions


Notation

- T - lifetime, time-to-event. (naturally, $T \geq 0$)
- $F(t) = P(T \leq t)$: cdf
- $S(t) = 1 - F(t) = P(T > t)$: Survival function
- $f(t)$ - density of T , $f(t) = \frac{dF(t)}{dt} = -\frac{dS(t)}{dt}$
- $P(a \leq T \leq b) = F(b) - F(a) = S(a) - S(b)$
- $h(t)dt = P(t \leq T \leq t + dt | T \geq t) = \frac{S(t) - S(t+dt)}{S(t)}$
- $h(t) = \lim_{dt \rightarrow 0} \left(\frac{S(t) - S(t+dt)}{dt} \cdot \frac{1}{S(t)} \right) = -\frac{S(t)'}{S(t)} = -(\log S(t))'$
- $h(t)$ is called hazard function

Lifetime Distributions

- $h(t) = -\frac{S(t)'}{S(t)} = \frac{f(t)}{S(t)}$

-  $f(t)dt = P(t \leq T \leq T + dt)$

-  $h(t)dt = P(t \leq T \leq T + dt | T \geq t)$

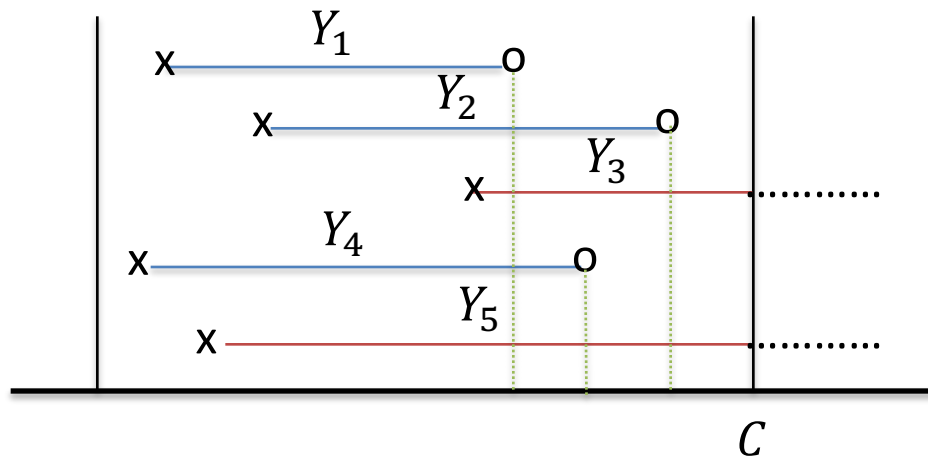
- Cumulative Hazard

$$H(t) = \int_0^t h(u) du = - \int_0^t (\log S(u))' du = -\log S(t) + 0$$

$$\Rightarrow S(t) = e^{-H(t)}$$

$S(t)$, $h(t)$ most popular summaries in time-to-event modeling

Censoring



Y_1, Y_2, Y_4 - fully observed

Y_3, Y_5 - censored

Censoring indicator: $\delta = 0$
(observed), $\delta = 1$ (censored)

Time	Y_1	Y_2	Y_3	Y_4	Y_5
δ	0	0	1	0	1


- Typical – right-censored data
- Censoring types
 - I. - censoring time fixed, number of observed random
 - II. - censoring time random, number of observed fixed
- Most common: right-censoring of type I


Likelihood with Censored Observations

$$Y_i \sim f(y_i|\theta), \quad i = 1, \dots, n$$

$$\delta_i = 0, \quad i = 1, \dots, k, \quad \delta_i = 1, \quad i = k + 1, \dots, n$$

$$L(\theta|y_1, \dots, y_n) = \prod_{i=1}^n (f(y_i|\theta))^{1-\delta_i} (S(y_i|\theta))^{\delta_i}$$


$$S(y_i|\theta) = P^\theta(Y_i > y_i)$$

- Bayesian inference about θ  $L(\theta|y_1, \dots, y_n) + \pi(\theta)$

Example 1:

$$Y_1, Y_2, \dots, Y_n \sim \mathcal{E}(\lambda)$$

Let $\delta_i = 0, \quad i = 1, \dots, k; \quad \delta_i = 1, \quad i = k + 1, \dots, n$

- What is (frequentist) estimator of λ ?

- If all are observed $\Rightarrow \frac{n}{\sum_{i=1}^n Y_i} = \frac{1}{\bar{Y}}$

- Shall we ignore censored data? If so,

$$\Rightarrow \hat{\lambda} = \frac{k}{\sum_{i=1}^k Y_i} \quad \text{[Wrong!]}$$

- Shall we consider censored as observed? If so,

$$\Rightarrow \frac{n}{\sum_{i=1}^n Y_i} = \frac{1}{\bar{Y}} \quad \text{[Wrong!]}$$

Example 1: (cont.)

$$Y_1, Y_2, \dots, Y_n \sim \mathcal{E}(\lambda)$$

Let $\delta_i = 0, \quad i = 1, \dots, k; \quad \delta_i = 1, \quad i = k + 1, \dots, n$

- The likelihood is $L(\theta|y_1, \dots, y_n) = \lambda^k e^{-(\lambda \sum_{i=1}^n Y_i)}$, so

$$\text{MLE} \Rightarrow \hat{\lambda} = \frac{k}{\sum_{i=1}^n Y_i} = \frac{k}{n\bar{Y}} \quad [\text{Correct!, as an exercise show this}]$$

Example 2:

Let: $Y_1 = 2, Y_2 = 3, Y_3 = 1^*, Y_4 = \frac{5}{2}, Y_5 = 3^*$;

Assume that: $Y_i \sim Wei(\nu, \lambda), \nu = \frac{3}{2}$.

- Using prior on $\lambda \sim Ga(2, 3)$, estimate λ .

- Note that $\begin{cases} f(y_i | \nu, \lambda) = \nu \lambda y_i^{\nu-1} e^{-\lambda y_i^\nu}, y_i \geq 0 \\ S(y_i | \nu, \lambda) = e^{-\lambda y_i^\nu}, y_i \geq 0 \end{cases}$

- The likelihood is:

$$\underbrace{\prod_{i=1}^k \nu \lambda y_i^{\nu-1} e^{-\lambda y_i^\nu}}_{\text{observed}} \underbrace{\prod_{i=k+1}^n e^{-\lambda y_i^\nu}}_{\text{censored}} = \nu^k \lambda^k \left(\prod_{i=1}^k y_i \right)^{\nu-1} e^{-\lambda \sum_{i=1}^n y_i^\nu}$$

Example 2: (cont.)

- The likelihood is: $\prod_{i=1}^k v \lambda y_i^{v-1} e^{-\lambda y_i^v} \prod_{i=k+1}^n e^{-\lambda y_i^v} = v^k \lambda^k \left(\prod_{i=1}^k y_i \right)^{v-1} e^{-\lambda \sum_{i=1}^n y_i^v}$

$$\Rightarrow L(\lambda | v, y_1, \dots, y_n) \propto \lambda^k e^{-\lambda \sum_{i=1}^n y_i^v}$$

$$\Rightarrow \pi(\lambda | \alpha, \beta) \propto \lambda^{\alpha-1} e^{-\beta \lambda}$$

$$\Rightarrow \pi(\lambda | v, y_1, \dots, y_n, \alpha, \beta) \propto \lambda^{k+\alpha-1} e^{-\lambda(\beta + \sum_{i=1}^n y_i^v)}$$

- For $k = 3$, $v = \frac{3}{2}$, $\alpha = 2$, $\beta = 3$, and $\sum_{i=1}^5 y_i^{3/2} = 18.1736$:

$$\Rightarrow \pi(\lambda | v, y_1, \dots, y_n, \alpha, \beta) \sim \text{Ga}(3 + 2, 18.1736 + 3)$$

$$\Rightarrow \hat{\lambda}_{\text{bayes}} = \frac{5}{21.1736} = 0.2361$$

Example 2: (cont.)

The screenshot shows the OpenBUGS software interface. The main window displays the following code:

```
EXAMPLE 2

model{
  for ( i in 1:n){
    y[i] ~ dweib(nu, lambda)C(censored[i],)
  }
  nu <- 3/2
  lambda ~ dgamma(2,3)
}

DATA
list( n=5, y=c(2, 3, NA, 2.5, NA), censored =c(0,0,1,0,3))

INITS
list( y = c(NA, NA, 2, NA, 4), lambda = 1 )
```

Below the code editor, there is a 'Node statistics' table:

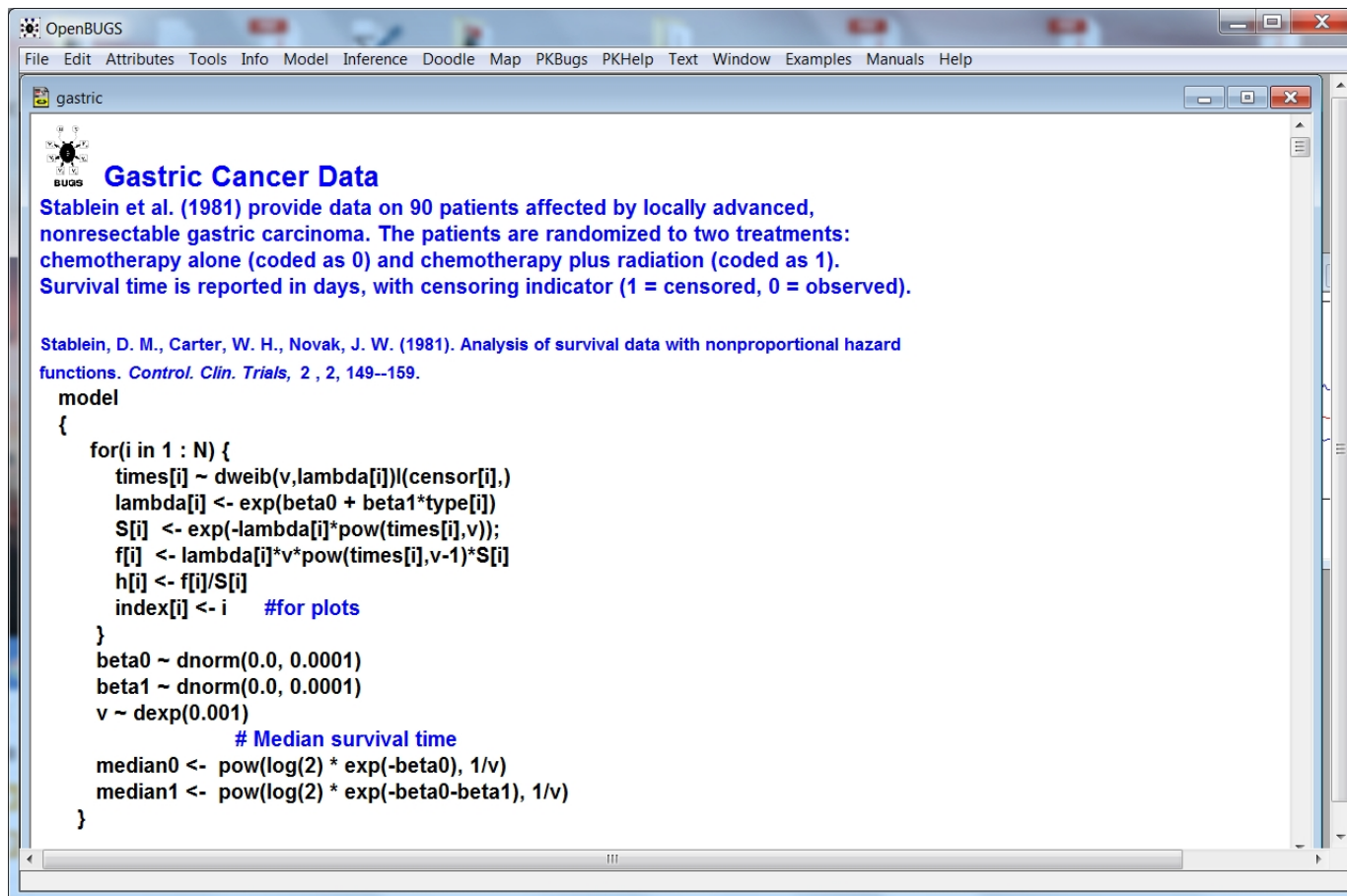
	mean	sd	MC_error	val2.5pc	median	val97.5pc	start	sample
lambda	0.2354	0.1053	4.224E-4	0.07657	0.2196	0.4825	1001	100000
y[3]	3.139	2.005	0.007552	1.07	2.598	8.379	1001	100000
vf5l	4.647	1.725	0.006847	3.041	4.124	9.268	1001	100000

On the right side, there are three tool windows:

- Sample Monitor Tool:** Shows a list of percentiles (2.5, 5, 10, 25, median, 75, 90, 95, 97.5) and buttons for diagnostics (clear, set, trace, jump, stats, density, bgr diag, history, accept, code, quantiles, auto cor).
- Specification Tool:** Contains buttons for 'check model', 'load data', 'compile', 'load inits', 'gen inits', and settings for 'num of chains' (1) and 'for chain' (1).
- Update Tool:** Contains settings for 'updates' (100000), 'refresh' (10000), 'update' (thin 1), 'iteration' (101000), and checkboxes for 'adapting' and 'over relax'.

example2.odc

Example 3:



Gastric Cancer Data

Stablein et al. (1981) provide data on 90 patients affected by locally advanced, nonresectable gastric carcinoma. The patients are randomized to two treatments: chemotherapy alone (coded as 0) and chemotherapy plus radiation (coded as 1). Survival time is reported in days, with censoring indicator (1 = censored, 0 = observed).

Stablein, D. M., Carter, W. H., Novak, J. W. (1981). Analysis of survival data with nonproportional hazard functions. *Control. Clin. Trials*, 2, 2, 149--159.

```
model
{
  for(i in 1 : N) {
    times[i] ~ dweib(v,lambda[i])|(censor[i],)
    lambda[i] <- exp(beta0 + beta1*type[i])
    S[i] <- exp(-lambda[i]*pow(times[i],v));
    f[i] <- lambda[i]*v*pow(times[i],v-1)*S[i]
    h[i] <- f[i]/S[i]
    index[i] <- i    #for plots
  }
  beta0 ~ dnorm(0.0, 0.0001)
  beta1 ~ dnorm(0.0, 0.0001)
  v ~ dexp(0.001)

  # Median survival time
  median0 <- pow(log(2) * exp(-beta0), 1/v)
  median1 <- pow(log(2) * exp(-beta0-beta1), 1/v)
}
```

gastric.odc

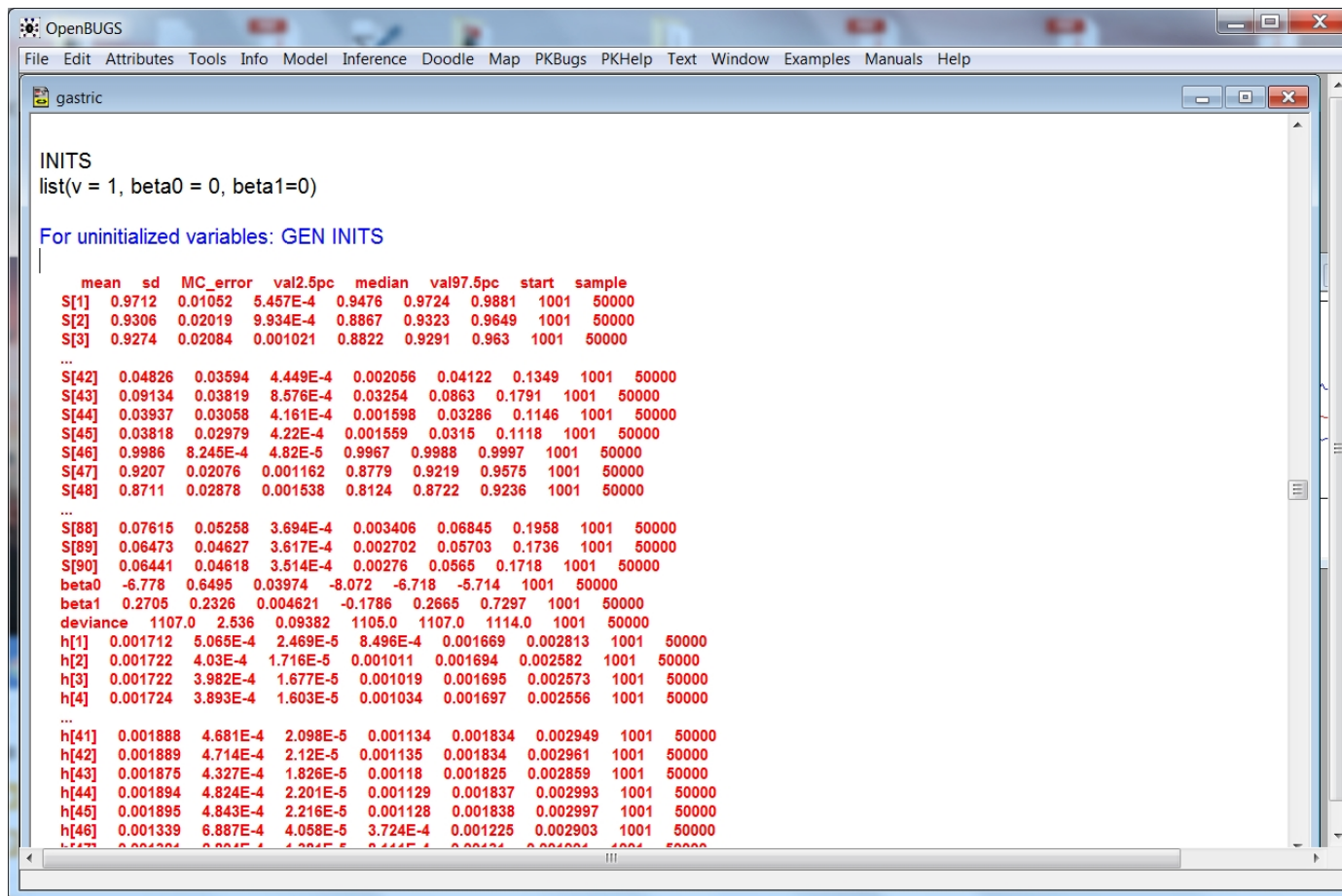
Example 3: (cont.)

The screenshot shows the OpenBUGS software interface. The main window displays a list of data for a gastric cancer dataset. The data is organized into columns representing different variables for 90 subjects. The variables include survival times, censoring status, and other clinical data. The data is presented in a text-based format, with values separated by commas and new lines. The interface includes a menu bar at the top with options like File, Edit, Attributes, Tools, Info, Model, Inference, Doodle, Map, PKBugs, PKHelp, Text, Window, Examples, Manuals, and Help. The title bar of the main window is labeled 'gastric'.

```
list( N=90, type=c(1,1,1,1,1,1,1,1,1,1, 1,1,1,1,1,1,1,1,1,1, 1,1,1,1,1,1,1,1,1,1,
1,1,1,1,1,1,1,1,1,1, 1,1,1,1,1,1,
0,0,0,0,0,0,0,0,0,0, 0,0,0,0,0,0,0,0,0,0, 0,0,0,0,0,0,0,0,0,0, 0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0), censor=c(0,0,0,0,0,0,0,0,0,0, 0,0,0,0,0,0,0,0,0,0, 0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0,0, 0, 882, 892, 1031, 1033, 1306, 1335,
0, 1452, 1472, 0, 0, 0, 0,
0, 0, 0, 0, 0, 0, 0, 0,
0, 0, 0, 0, 381, 0, 0,
0, 0, 0, 0, 0, 0, 0,
529, 0, 0, 0, 0, 0, 0,
0, 0, 0, 945, 0, 0, 1180,
0, 0, 1277, 1397, 1512, 1519),
times=c( 17, 42, 44, 48, 60, 72, 74,
95, 103, 108, 122, 144, 167, 170,
183, 185, 193, 195, 197, 208, 234,
235, 254, 307, 315, 401, 445, 464,
484, 528, 542, 567, 577, 580, 795,
855, NA, NA, NA, NA, NA, NA,
1366, NA, NA, 1, 63, 105, 129,
182, 216, 250, 262, 301, 301, 342,
354, 356, 358, 380, NA, 383, 383,
388, 394, 408, 460, 489, 499, 524,
NA, 535, 562, 675, 676, 748, 748,
778, 786, 797, NA, 955, 968, NA,
1245, 1271, NA, NA, NA, NA) )
```

gastric.odc

Example 3: (cont.)



gastric

INITs
list(v = 1, beta0 = 0, beta1=0)

For uninitialized variables: GEN INITs

	mean	sd	MC_error	val2.5pc	median	val97.5pc	start	sample
S[1]	0.9712	0.01052	5.457E-4	0.9476	0.9724	0.9881	1001	50000
S[2]	0.9306	0.02019	9.934E-4	0.8867	0.9323	0.9649	1001	50000
S[3]	0.9274	0.02084	0.001021	0.8822	0.9291	0.963	1001	50000
...								
S[42]	0.04826	0.03594	4.449E-4	0.002056	0.04122	0.1349	1001	50000
S[43]	0.09134	0.03819	8.576E-4	0.03254	0.0863	0.1791	1001	50000
S[44]	0.03937	0.03058	4.161E-4	0.001598	0.03286	0.1146	1001	50000
S[45]	0.03818	0.02979	4.22E-4	0.001559	0.0315	0.1118	1001	50000
S[46]	0.9986	8.245E-4	4.82E-5	0.9967	0.9988	0.9997	1001	50000
S[47]	0.9207	0.02076	0.001162	0.8779	0.9219	0.9575	1001	50000
S[48]	0.8711	0.02878	0.001538	0.8124	0.8722	0.9236	1001	50000
...								
S[88]	0.07615	0.05258	3.694E-4	0.003406	0.06845	0.1958	1001	50000
S[89]	0.06473	0.04627	3.617E-4	0.002702	0.05703	0.1736	1001	50000
S[90]	0.06441	0.04618	3.514E-4	0.00276	0.0565	0.1718	1001	50000
beta0	-6.778	0.6495	0.03974	-8.072	-6.718	-5.714	1001	50000
beta1	0.2705	0.2326	0.004621	-0.1786	0.2665	0.7297	1001	50000
deviance	1107.0	2.536	0.09382	1105.0	1107.0	1114.0	1001	50000
h[1]	0.001712	5.065E-4	2.469E-5	8.496E-4	0.001669	0.002813	1001	50000
h[2]	0.001722	4.03E-4	1.716E-5	0.001011	0.001694	0.002582	1001	50000
h[3]	0.001722	3.982E-4	1.677E-5	0.001019	0.001695	0.002573	1001	50000
h[4]	0.001724	3.893E-4	1.603E-5	0.001034	0.001697	0.002556	1001	50000
...								
h[41]	0.001888	4.681E-4	2.098E-5	0.001134	0.001834	0.002949	1001	50000
h[42]	0.001889	4.714E-4	2.12E-5	0.001135	0.001834	0.002961	1001	50000
h[43]	0.001875	4.327E-4	1.826E-5	0.00118	0.001825	0.002859	1001	50000
h[44]	0.001894	4.824E-4	2.201E-5	0.001129	0.001837	0.002993	1001	50000
h[45]	0.001895	4.843E-4	2.216E-5	0.001128	0.001838	0.002997	1001	50000
h[46]	0.001339	6.887E-4	4.058E-5	3.724E-4	0.001225	0.002903	1001	50000

gastric.odc

Example 3: (cont.)

OpenBUGS

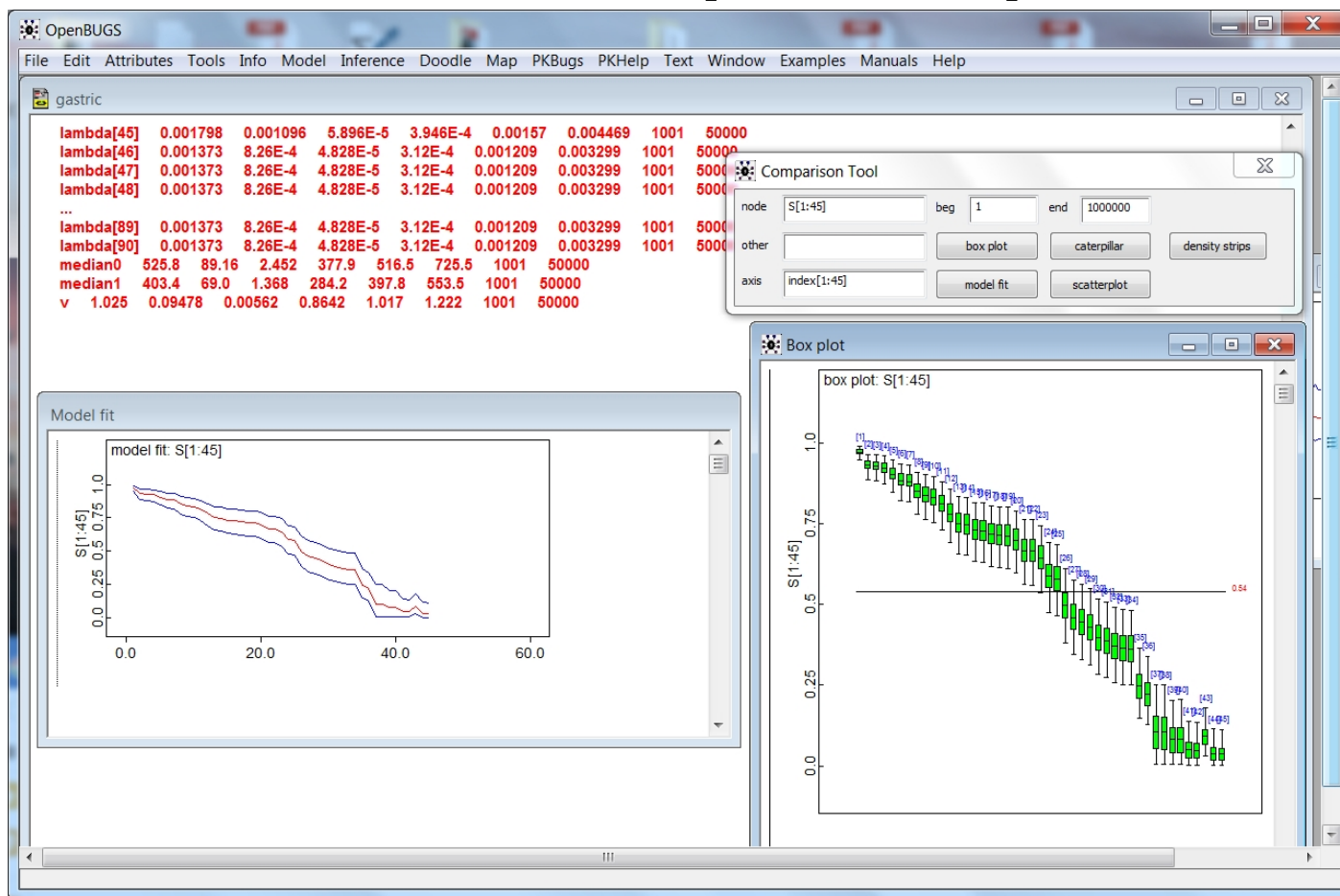
File Edit Attributes Tools Info Model Inference Doodle Map PKBugs PKHelp Text Window Examples Manuals Help

gastric

h[4]	0.001724	3.893E-4	1.603E-5	0.001034	0.001697	0.002556	1001	50000
...								
h[41]	0.001888	4.681E-4	2.098E-5	0.001134	0.001834	0.002949	1001	50000
h[42]	0.001889	4.714E-4	2.12E-5	0.001135	0.001834	0.002961	1001	50000
h[43]	0.001875	4.327E-4	1.826E-5	0.00118	0.001825	0.002859	1001	50000
h[44]	0.001894	4.824E-4	2.201E-5	0.001129	0.001837	0.002993	1001	50000
h[45]	0.001895	4.843E-4	2.216E-5	0.001128	0.001838	0.002997	1001	50000
h[46]	0.001339	6.887E-4	4.058E-5	3.724E-4	0.001225	0.002903	1001	50000
h[47]	0.001321	2.804E-4	1.381E-5	8.111E-4	0.00131	0.001901	1001	50000
h[48]	0.001331	2.498E-4	1.056E-5	8.732E-4	0.001321	0.001846	1001	50000
h[49]	0.001336	2.402E-4	9.249E-6	8.933E-4	0.001325	0.001832	1001	50000
...								
h[88]	0.001445	3.603E-4	1.262E-5	8.484E-4	0.001408	0.002249	1001	50000
h[89]	0.001449	3.673E-4	1.315E-5	8.452E-4	0.001411	0.002265	1001	50000
h[90]	0.001449	3.677E-4	1.32E-5	8.448E-4	0.001409	0.002268	1001	50000
lambda[1]	0.001798	0.001096	5.896E-5	3.946E-4	0.00157	0.004469	1001	50000
lambda[2]	0.001798	0.001096	5.896E-5	3.946E-4	0.00157	0.004469	1001	50000
...								
lambda[44]	0.001798	0.001096	5.896E-5	3.946E-4	0.00157	0.004469	1001	50000
lambda[45]	0.001798	0.001096	5.896E-5	3.946E-4	0.00157	0.004469	1001	50000
lambda[46]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
lambda[47]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
lambda[48]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
...								
lambda[89]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
lambda[90]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
median0	525.8	89.16	2.452	377.9	516.5	725.5	1001	50000
median1	403.4	69.0	1.368	284.2	397.8	553.5	1001	50000
v	1.025	0.09478	0.00562	0.8642	1.017	1.222	1001	50000

gastric.odc

Example 3: (cont.)



gastric.odc