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Y. Xie

A. M. Parkhurst

T. L. Mader

J. B. Gaughan

See next page for additional authors

Author Information

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Comparison of SAS Proc Nlin and Nlmixed for Parameter Estimation in PET Model

Y. Xie[1], A. M. Parkhurst[1], T. L. Mader[2], and J. B. Gaughan[3]

[1]Department of Biometry, University of Nebraska at Lincoln

[2]Department of Animal Science, University of Nebraska at Lincoln

[3]School of Animal Studies, The University of Queensland, Gatton, Australia

ABSTRACT

Cattle body temperatures were measured under semi-controlled hot cyclic chamber temperatures. The four-parameter nonlinear PET model, is used to estimate body temperature in cattle challenged by heat stress. For each steer, the parameters can be estimated by the Nlin procedure and the sensitivity of each animal can be studied. It is also desirable to generalize the results by using the Nlmixed procedure to combine both the fixed and random effects. When comparing the results from the two procedures, we found heterogeneity among animals and/or days caused convergence problems for proc Nlmixed. Simulation studies were used to study how deviations from homogeneity effected the accuracy of parameter estimates, coverage of confidence intervals, and measures of nonlinear behavior when using the PET model to describe the dynamics of heat stress in cattle.

Key words: Nlin, Nlmixed, Parameter estimation, PET model

1. INTRODUCTION

Environmental discomfort in the form of excessive heat load (heat stress) can represent a sizeable economic loss to cattle feeders through reduced and, in extreme cases, death of cattle. When cattle are under heat stress, air temperature, Ta, appears to be a principal driving force influencing body temperature. A four parameter model, termed the PET model (Parkhurst et al, 2001), is used to estimate body temperature in cattle challenged by hot cyclic chamber temperatures. The traditional method is to fit each steer - day combination separately by Nlin procedure and obtain the parameter estimates for each steer for a given day. The inference of parameter estimates is based on an individual animal. The usual question asked by animal scientists is: Can we fit a general model for all the steers and days to get parameter estimates which represent a boarder scope of inference scope for a population rather than estimates for each individual animal. Proc Nlinmix [SAS, 1999] provides a way to combine the fixed and random effects, fit all steers simultaneously and get parameter estimates provided all steers come from the same population. Thus proc Nlmixed provides a broader scope of inference, estimates of variation among animals and more precise parameter estimates.

When Proc Nlmixed was used to estimate the parameters, the following questions arose: 1) Are the parameter estimates obtained from Nlmixed and Nlin procedures comparable? 2) If these animals come from different populations, how does that influence the parameter estimates from these two procedures? 3) Are experimental units (animals) from the same population, i.e. how can deviations from homogeneity be identified?

To answer these questions, cattle body temperatures driven by Ta from semi-controlled temperature chambers were used to compare the results of parameter estimates from Nlin and Nlmixed procedures. This data was also used to provide a design structure for two simulation studies.

2. EXPERIMENTAL DESIGN

A metabolism trial was conducted during the late spring and early summer at the University of Queensland, Gatton College, Department of Animal Production facilities, Australia. Six *Bos taurus* (Hereford) steers were randomly assigned to individual stalls (9.8 ft x 3.3 ft). The metabolism unit was divided into two separate chambers, each containing three stalls. These chambers were separated by an insulated partition. One chamber had the capability of being heated to temperatures above 100 ^{0}F (HOT) while the other chamber could be maintained at or near thermoneutral (TNL) conditions. During the trial, the HOT group of steers was exposed to excessive heat load (heat stress) by heating the HOT chamber from approximately 72 ^{0}F (22 °C) to temperatures around 100 ^{0}F at daytime, and gradually allowed to cool down to thermoneutral conditions at night. Cattle body temperatures were obtained via an 8-inch rectal probe with a thermistor mounted in the tip. Body temperatures °C recorded at ten-minute time stamped intervals for the duration of the trial using a data logger. Hourly mean body temperatures were calculated based on these measurements.

This experiment was run for 19 days and divided to three periods. Cattle were fed different diets for each period. For period 1 (day 1 to day 6), a low energy diet (40% roughage) was given to the cattle. A medium energy diet (25% roughage) was given during period 2 (day 6 to day 11) and a high energy diet (10% roughage) was given during the last period (day 11 to 19). In this study, we used the data from period 1, semi-controlled heat stress situation and compared the parameter estimates from Nlin and Nlmixed procedures using PET model.

3. MODEL EQUATION

This model was derived by Parkhurst, Eskridge and Travnicek (Parkhurst et al, 2001). It is a modification of Newton's law of cooling with a sinusoidal function for Ta.

The chamber temperature, Ta, is modeled by

$$T_a = \mu_a + A_a \sin\{\omega(t - \phi)\}$$

where μ_a = mean, A_a is amplitude, ω is frequency, and ϕ is phase angle.

The body temperature of the animal, T_B, is modeled by

$$\mathbf{T_B = \mu_B + A_B \sin\{\omega(t - \phi) - \tau\} - [\gamma\mu_a - T_{Binitial} - A_B \sin\{\omega(t - \phi) - \tau\}]e^{-Kt}}$$

where μ_B is mean for T_B,

$$A_B = \frac{\gamma K A_a}{\sqrt{\omega^2 + K^2}}$$ is amplitude,

$$\tau = \frac{\tan^{-1}(\frac{\omega}{K})}{\omega}$$ is the lag or delay.

The thermal constant, K, hr^{-1}, characterizes how rapidly T_B adjusts to changes in Ta. Smaller K values indicate larger delays in effect of Ta, i.e.longer time for cattle to respond to heat stress. The thermal constant can be converted to the lag τ.

The parameter τ represents the time it takes an animal to response to the heat stress. Frequently τ is used instead of K to determine if there is a delay in cattle body temperature due to hot ambient temperature and characterize the time for cattle to response to such heat stress.

The thermal driving ratio, γ, which can be thought of as the proportion of variation in T_B relative to variation in T_a. Larger γ values indicate more influence of Ta on T_B which indicates that T_B is "thermally driven".

The thermal gradient between T_B and adjusted T_a is the parameter Δ where adjusted Ta is the air temperature adjusted by thermal driving ratio. $\Delta = \mathbf{T_B} - \gamma \mathbf{T_a}$.

Both the Nlin and Nlmixed procedures used the above model equations (Tables 8 and 9). In the Nlmixed procedure, the steers were treated as a random sample from a population, the steer initial body temperature, $T_{Binitial}$, was treated as a random effect and steer was treated as the subject.

4. RESULTS AND DISCUSSIONS

Nlin and Nlmixed procedures were used to estimate the PET model parameters for the original data set. Data were analyzed for acute and chronic phases of the heat challenge environment for day 2, 3 and 4 in period 1. The results are shown in Table 1.1 to 1.3. These results provide a convenient way to compare the individual steer parameter estimates from Nlin and the aggregated estimates from the Nlmixed procedure. The estimates were consistent for Day 2 (Table 1.1). When Nlmixed procedure is employed, the standard errors of parameter estimates are usually smaller than the standard errors from Nlin procedure. Nlmixed procedure can give more precise parameter estimates in this case. For Day 4 (Table 1.3), the estimates were not consistent for these two procedures. The results from Nlmixed procedure do not represent any of these three steers possibly due to the heterogeneity among the steers. The variance estimate for the random effect was a problem for day 3, although it gave the similar results for other parameter estimates in the model (Table 1.2). The standard errors of parameter estimates (shown in each table below the parameter estimates) are similar for both the procedures.

Intrinsic, IN, and parameter-effect, PE, curvatures (Bates, D. M. and Watts, D.L.1980,1988) were measured for the original data sets and compared to the 0.4 crucial level. The standardized intrinsic curvatures, shown in Table 2, indicate the planarity assumption does not hold for Day 4's data. However, planarity seems acceptable for Day 2 and Day 3's data sets. The standardized parameter-effect curvatures indicate that the linear assumption does not hold in all but one these analyses. All the parameter-effect curvatures are greater than 0.4 except for day 3 steer 11. The violation of this assumption might be due to the properties of a single factor because PE measures the maximum curvature associated with all the parameters. So it is reasonable to examine each parameter separately. The nonlinear behaviors for each parameter including Box's bias, percentage of Box's bias (Box, M. J. 1972), excess variance, percentage of excess variance (Lowry, R. and Morton R. 1983) and Hougaard skewness (Hougaard, P. 1985) were also examined. The results were shown in Tables 3.1 to 3.3. These results indicated that the linear assumption for the thermal constant K and initial body temperature $T_{Binitial}$ hold very well for Day 2 and Day 3 while the percentage of excess variance and Hougaard skewness appear troublesome for Day 4. The linear assumptions for thermal driving ratio (and gradient) do not hold for all the data sets. So the large parameter-effect curvature may be due to the violation of linear assumption for these two parameters. In the future reparameterization may be investigated to reduce the parameter-effect curvature or another experimental design, i.e. using the half-hourly data rather than hourly data should be studied to find better nonlinear behavior.

A simulation study was used to compare the estimates from Nlmixed and Nlin for two values of the lag (τ=3 or τ=4). The design structure for the simulation is based on parameter estimates from the metabolism trial. All 400 data sets were generated based on identical values of $T_{Binitial}=39.8$, $\Delta=35.0$, $\gamma=0.15$ and $\sigma^2_{TB}=0.008$ based on PET model and the same air temperature ($\mu_a = 32.7$, $A_a = 7.5$ and $\phi = 10.8$). Half of these data sets had K=0.262 (lag τ=3) and the other half had K=0.151 (τ=4). Each data set was analyzed by Nlin procedure. The parameter estimates, their standard errors and 95% confidence intervals were obtained. Intrinsic curvature, parameter-effect curvature and nonlinear behaviors, statistics (Box's bias, percentage of Box's bias, excess variance, percentage of excess variance and Hougaard skewness) were obtained for each data set. The 200 data sets with τ=3 or τ=4 were each analyzed by Nlmixed procedure. Then all 400 data sets were analyzed by proc Nlmixed. The parameter estimates, their standard errors and 95% confidence intervals were obtained from this procedure. The results for Nlmixed were used to compare with the results from Nlin.

The parameter estimates from these two procedures are shown in Table 4. The parameter estimates from the Nlin procedure are the average of 200 parameter estimates from the 200 data sets. The standard errors of parameter estimates were the square root of the average of 200 variance estimates for each parameter. The parameter estimates from Nlmixed procedure had only one value and their standard errors were given by the procedure. Table 4 shows if the data are from the same population the Nlin and Nlmixed estimates are consistent with each other. Moreover confidence intervals constructed from the SE's cover the true values of parameters. For Nlin procedure, the probability of 95% confidence interval of parameter estimates covered the true parameter was 86.5 - 97%. Proc Nlmixed gives more precise estimates; but when the data from the two populations are combined, the parameter estimates from Nlmixed were far from the true value and did not represent either of the two populations.

The intrinsic curvature, parameter-effect curvature and other nonlinear behavior parameters for the simulated data sets from Nlin procedure were shown in Table 5. These values are the averages of 200 individual values and their standard errors are obtained from univariate analyses. Some standard errors are very large due to the existence of extreme values for the nonlinear behavior parameters. The results indicate that the linear assumption holds better for τ=3 cases than for τ=4 cases.

In order to study the distribution of the parameter estimate, a univariate analyse was used to get variance and skewness for each parameter distribution. The percentage bias of parameter estimates from the true values, their variances and skewness for each parameter were shown in Table 6. The bias for a parameter is the differences between the average parameter estimate and the true value of the parameter that was set for the simulation. The percent bias of parameter estimate equals the bias divided by the true value of the parameter. The results show that the percentage bias from the true values are very small but the probability of coverage for the 95% confidence intervals was lower than 95% for most parameters especially initial body temperature. The analysis also showed, even when the data comes from the same population, τ, K and $T_{binitial}$ are normally distributed while Δ and γ are not. The histograms of these parameter estimate distributions are shown in Figure1 for $\tau = 3$ and Figure 2 for $\tau = 4$.

In order to identify homogeneity among steers, bootstrapping residuals (fixed-X bootstrap sampling) was used to estimate the precision of the parameters estimated from the metabolic trial. Bootstrap method was first discussed by Efron [Efron, B. 1982, 1987 and 1993] and was used as a re-sampling method. Bootstrapping residuals called fixed-X bootstrap sampling by Neter (Neter, J et al 1996) is based on using an appropriate model to get the predicted value and residual for each observation. The residuals are then randomly assigned back to predicted values to get the new observations. These new observations were used to fit the model again and get another set of parameter estimates. The bootstrap method provides another way to determine the reliability of a parameter. The prior conditions for this method are: a good model for data, errors with constant variance and a fixed predictor X. The bootstrap method used is as the following procedure. First, the model was fit for each steer separately. The predicted values and residuals were recorded. Second, all the residuals were randomly assigned back to the predicted values. This process was repeated 20 times for the 3 steers on diet 1 day 4. These data sets were analyzed by using Nlin and Nlmixed procedure and the parameter estimates were obtained by PET model. The bootstrapping results (Table 7) indicated that all the steers come from different populations. When the steers come from the same population, the parameter estimates from Nlin procedure are similar to the results of Nlmixed procedure. The parameter estimates from Nlmixed procedure are more accurate than the estimates from Nlin procedure but only if the steer come from the same population.

5. CONCLUSIONS

Nlmixed procedure provides the possibility of fitting all steers in a general model giving more precision of parameter estimates and a boarder scope of inference. If all steers come from the same population the Nlmixed results are consistent with the results from Nlin procedure. Both the simulation study and the bootstrapping method gave the same conclusions.

Homogeneity is an important condition to get reliable estimates from the Nlmixed procedure. When the population is not homogeneous, Nlmixed may fail to converge and even when it converges, the simulation study showed that Nlmixed converged to unreasonable values. The parameter estimates did not represent either of the two populations in this case. Therefore checking homogeneity among the experimental units (in this case steers) is a crucial issue to address before using the Nlmixed procedure.

Bootstrap sampling is a promising way to check for homogeneity. In this study, bootstrapping residuals sampling was used to generate the bootstrap samples. Evaluating the precision of the parameter estimates allowed us to detect lack of homogeneity among the steers. The results from bootstrapping residuals can help us select the appropriate procedure for data analysis.

In summary, the Nlmixed procedure is prefered if the steers come from the same population. The parameter estimates from Nlin and Nlmixed procedures were consistent. Nlmixed procedure can give more precise estimates than the Nlin procedure which implies smaller estimated standard errors for the parameter estimates and thus narrower confidence intervals. The inference from parameter estimates based on the Nlmixed procedure is useful for the whole population of steers rather than for an individual animal. However, Nlmixed results can be seriously misleading if the steers are not from the same population.

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Table 1.1 Parameter Estimates (Diet1 Day2)

Parameter	MSE	τ (SE)	K (SE)	$T_{binitial}$ (SE)	Δ (SE)	γ (SE)
Steer 11	0.0244	2.80 (0.4770)	0.2903 (0.0729)	39.72 (0.1848)	36.74 (0.3723)	0.0922 (0.0133)
Steer 12	0.0140	2.70 (0.3556)	0.3061 (0.0577)	39.58 (0.1454)	36.63 (0.2727)	0.0894 (0.0097)
Steer 13	0.0138	2.86 (0.5473)	0.2819 (0.0810)	39.12 (0.1233)	37.36 (0.2502)	0.0660 (0.0660)
Nlmixed		2.84 (0.2867)	0.2851 (0.0430)	39.46 (0.1548)	36.89 (0.1982)	0.0835 (0.0071)

Table 1.2 Parameter Estimates (Diet1 Day3)

Parameter	MSE	τ (SE)	K SE)	$T_{binitial}$ (SE)	Δ (SE)	γ (SE)
Steer 11	0.0138	2.62 (0.2976)	0.3196 (0.0508)	39.39 (0.1284)	36.15 (0.2361)	0.1159 (0.0082)
Steer 12	0.0196	3.18 0.3606)	0.2383 (0.0452)	39.67 (0.1442)	35.57 (0.4105)	0.1303 (0.0143)
Steer 13	0.0058	2.95 (0.3498)	0.2685 (0.0492)	39.56 (0.0896)	37.36 (0.2125)	0.0623 (0.0072)
Nlmixed*		2.91 (0.3410)	0.2739 (0.0489)	39.54 (0.1230)	36.40 (0.2861)	0.1015 (0.0099)

* The variance of random effect can not be estimated and is set to lower bound.

Table 1.3 Parameter Estimates (Diet1 Day4)

Parameter	MSE	τ (SE)	K (SE)	$T_{binitial}$ (SE)	Δ (SE)	γ (SE)
Steer 11	0.0192	4.17 (0.3371)	0.1356 (0.0293)	39.94 (0.1139)	34.19 (0.7529)	0.1844 (0.0249)
Steer 12	0.0188	4.54 (0.3666)	0.1054 (0.0292)	39.63 (0.1074)	33.33 (1.1945)	0.2016 (0.0397)
Steer 13	0.0160	3.71 (0.3899)	0.1789 (0.0392)	39.59 (0.1155)	35.78 (0.4849)	0.1166 (0.0157)
Nlmixed		5.65 (0.2680)	0.0240 (0.0185)	39.58 (0.1606)	21.71 (12.160)	0.6022 (0.4145)

Table 2. Standardized Maximum for Intrinsic, IN, and Parameter-effect, PE, Curvature

Day	Steer ID	IN	PE
Day 2	11	0.09154	0.7087
	12	0.08439	0.4831
	13	0.08313	0.8168
Day 3	11	0.05402	0.2802
	12	0.02650	0.6334
	13	0.03003	0.5327
Day 4	11	0.78700	1.9040
	12	1.32388	2.6767
	13	0.39752	1.5716

Table 3.1 Nonlinear Behavior parameters (Diet1 Day2)

Steer ID	Parameter	Box's Bias	PCT of Box's Bias	Asymtotic Variance	Excess Variance	PCT of Excess Variance	Hougaard Skewness
11	K	0.0000	0.0099	0.0000	0.0000	1.1282	0.0711
	$T_{binitial}$	-0.0006	-0.0016	0.0959	0.0007	0.6988	-0.0062
	Δ	1.0224	2.7824	29.996	2.8746	9.5832	1.1337
	γ	-0.0364	-39.532	0.0370	0.0036	9.8387	-1.1469
12	K	0.0000	0.0027	0.0000	0.0000	0.9372	0.0258
	$T_{binitial}$	-0.0007	-0.0018	0.0584	0.0003	0.5964	-0.0095
	Δ	0.5120	1.3976	16.074	0.8029	4.9953	0.7768
	γ	-0.0182	-20.418	0.0198	0.0010	5.1137	-0.7855
13	K	0.0000	0.0111	0.0000	0.0000	0.9659	0.1036
	$T_{binitial}$	-0.0004	-0.0010	0.0529	0.0003	0.5709	-0.0050
	Δ	1.2966	3.4704	35.507	4.3590	12.276	1.3160
	γ	-0.0461	-69.898	0.0440	0.0055	12.518	-1.3268

Table 3.2 Nonlinear Behavior parameters (Diet1 Day3)

Steer ID	Parameter	Box's Bias	PCT of Box's Bias	Asymtotic Variance	Excess Variance	PCT of Excess Variance	Hougaard Skewness
11	K	-0.0000	-0.0012	0.0000	0.0000	0.3712	-0.0123
	$T_{binitial}$	-0.0010	-0.0025	0.0585	0.0001	0.2426	-0.0141
	Δ	0.2081	0.5758	7.6137	0.1442	1.8945	0.4635
	γ	-0.0071	-6.1391	0.0086	0.0002	1.9524	-0.4699
12	K	0.0000	0.0180	0.0000	0.0000	0.1901	0.1395
	$T_{binitial}$	0.0006	0.0015	0.0623	0.0000	0.0398	0.0100
	Δ	0.7196	2.0231	17.7739	1.2281	6.9096	1.0366
	γ	-0.0245	-18.792	0.0198	0.0014	7.1889	-1.0528
13	K	0.0000	0.0046	0.0000	0.0000	0.1307	0.06905
	$T_{binitial}$	-0.0002	-0.0006	0.0205	0.0000	0.0642	-0.0059
	Δ	0.6020	1.6115	16.422	0.9008	5.4855	0.8984
	γ	-0.0205	-32.840	0.0186	0.0010	5.5908	-0.9049

Table 3.3 Nonlinear Behavior parameters (Diet1 Day4)

Steer ID	Parameter	Box's Bias	PCT of Box's Bias	Asymtotic Variance	Excess Variance	PCT of Excess Variance	Hougaard Skewness
11	K	-0.0001	-0.0498	0.0000	0.0000	87.560	-0.2296
	$T_{binitial}$	-0.0316	-0.0791	0.0377	0.0221	58.720	-0.5880
	Δ	1.9470	5.6939	47.084	49.355	104.82	1.7111
	γ	-0.0604	-32.736	0.0412	0.0438	106.17	-1.7856
12	K	-0.0004	-0.3863	0.0000	0.0000	259.74	-1.4171
	$T_{binitial}$	-0.0716	-0.1807	0.0288	0.051	177.04	-1.4102
	Δ	1.5613	4.6934	68.611	176.25	256.88	1.1388
	γ	-0.0510	-25.300	0.0585	0.151	257.68	-1.2662
13	K	0.0001	0.0431	0.0000	0.0000	22.409	0.2738
	$T_{binitial}$	-0.0079	-0.0200	0.0404	0.0057	14.1721	-0.1462
	Δ	2.3181	6.4789	46346	21.898	47.248	2.0524
	γ	-0.0714	-61.197	0.0422	0.0203	48.239	-2.0890

Table 4. The Parameter Estimates from 200 Simulated Data Sets

Parameter		τ	K	$T_{binitial}$	Δ	γ
True Value		3.00 or 4.00	0.262 or 0.151	39.80	35.00	0.1500
τ=3*	Estimate	2.99	0.2664	39.83	34.90	0.1501
	SE	(0.256)	(0.036)	(0.145)	(0.340)	(0.011)
	%Coverage of CI	93.5	93.5	89.5	97.0	95.0
τ =4*	Estimate	3.98	0.1551	39.83	34.76	0.1547
	SE	(0.380)	(0.035)	(0.121)	(0.826)	(0.027)
	%Coverage of CI	91.5	92.0	86.5	93.5	91.5
τ =3**	Estimate	2.98	0.2648	39.82	34.93	0.1490
	SE	(0.018)	(0.003)	(0.013)	(0.024)	(0.001)
τ =4**	Estimate	3.97	0.1539	39.82	34.96	0.1479
	SE	(0.027)	(0.003)	(0.011)	(0.049)	(0.001)
Combined Both Values**	Estimate	3.39	0.2127	39.82	35.12	0.1429
	SE	(0.018)	(0.002)	(0.011)	(0.026)	(0.001)

* The parameter estimates are the average of 200 estimates.
**Parameter estimates are from Nlmixed procedure.

Table 5. The Curvatures and Nonlinear Behaviors for 200 Simulated Data Sets

	IN (SE)	PE (SE)	Parameter	PCT of Box's Bias (SE)	PCT of Excess Variance (SE)	Hougaard Skewness (SE)
τ =3	0.0536 (0.0471)	0.5254 (0.2166)	K	0.0128 (0.0125)	0.7602 (1.9445)	0.0897 (0.0730)
			$T_{binitial}$	-0.0006 (0.0024)	0.4313 (1.2004)	-0.0019 (0.0138)
			Δ	1.4349 (0.9479)	5.1531 (4.9557)	0.7923 (0.2954)
			γ	-10.075 (6.2204)	5.3746 (5.1312)	-0.8081 (0.3023)
τ=4	0.7368 (0.5457)	1.9844 (0.9954)	K	-0.1497 (0.5799)	126.58 (218.87)	-0.3608 (1.1253)
			$T_{binitial}$	-0.0822 (0.1052)	85.42 (148.86)	-0.5999 (0.7088)
			Δ	5.7200 (4.1510)	138.76 (188.75)	0.7471 (-0.3608)
			γ	-42.841 (23.310)	139.44 (186.50)	-1.7330 (0.7039)

Table 6. The %Bias, Variance and Skewness for Distribution of Parameter Estimates

	Parameter	τ	K	$T_{Binitial}$	Δ	γ
τ=3*	%Bias	-0.33	1.75	0.075	-0.286	0.067
	Variance	0.079	0.001	0.034	0.107	0.0001
	Skewness	0.146	0.210	0.329	-0.117	0.111
τ=4*	%Bias	-0.40	2.65	0.075	-0.686	3.13
	Variance	0.185	0.001	0.027	0.856	0.0009
	Skewness	0.249	0.107	0.256	-1.506	1.532
τ=3**	%Bias	-0.67	1.14	0.050	-0.200	-0.666
τ=4**	%Bias	-0.75	1.85	0.050	0.114	-1.400

* The results are from Nlin procedure.
**The results are from Nlmixed procedure.

Table 7. Parameter Estimates from Modified Bootstraps Simulate Data Sets (20/steer)

Parameter	τ (SE)	K (SE)	$T_{Binitial}$ (SE)	Δ (SE)	γ (SE)
Steer 11*	4.12 (0.301)	0.1413 (0.027)	39.98 (0.108)	34.12 (0.723)	0.1862 (0.024)
Steer 12*	4.67 (0.333)	0.0959 (0.026)	39.63 (0.096)	32.53 (1.531)	0.2281 (0.051)
Steer 13*	3.61 (0.360)	0.1905 (0.038)	39.59 (0.110)	35.83 (0.437)	0.1149 (0.014)
Steer 11**	4.12 (0.066)	0.1407 (0.006)	39.98 (0.024)	34.21 (0.149)	0.1831 (0.005)
Steer 12**	4.66 (0.075)	0.0957 (0.006)	39.63 (0.021)	32.87 (0.289)	0.2168 (0.009)
Steer 13**	3.61 (0.078)	0.1890 (0.008)	39.59 (0.024)	35.88 (0.092)	0.1133 (0.003)

*Parameter estimates are the average of 20 individual estimates from Nlin Procedure.
** Parameter estimates are from Nlmixed procedure.

Figure 1. Histogram of Parameters (τ, K, Tinitial, Δ and γ when τ=3)

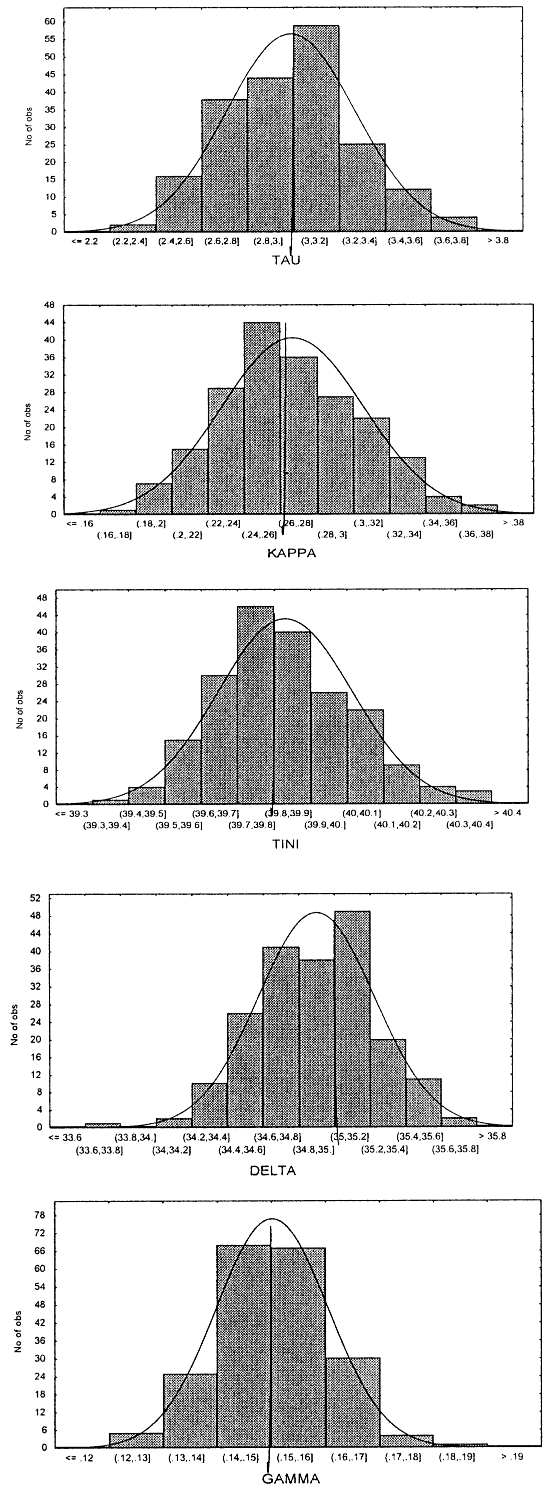

Figure 2. Histogram of Parameters (τ, K, Tinitial, Δ and γ when τ=4)

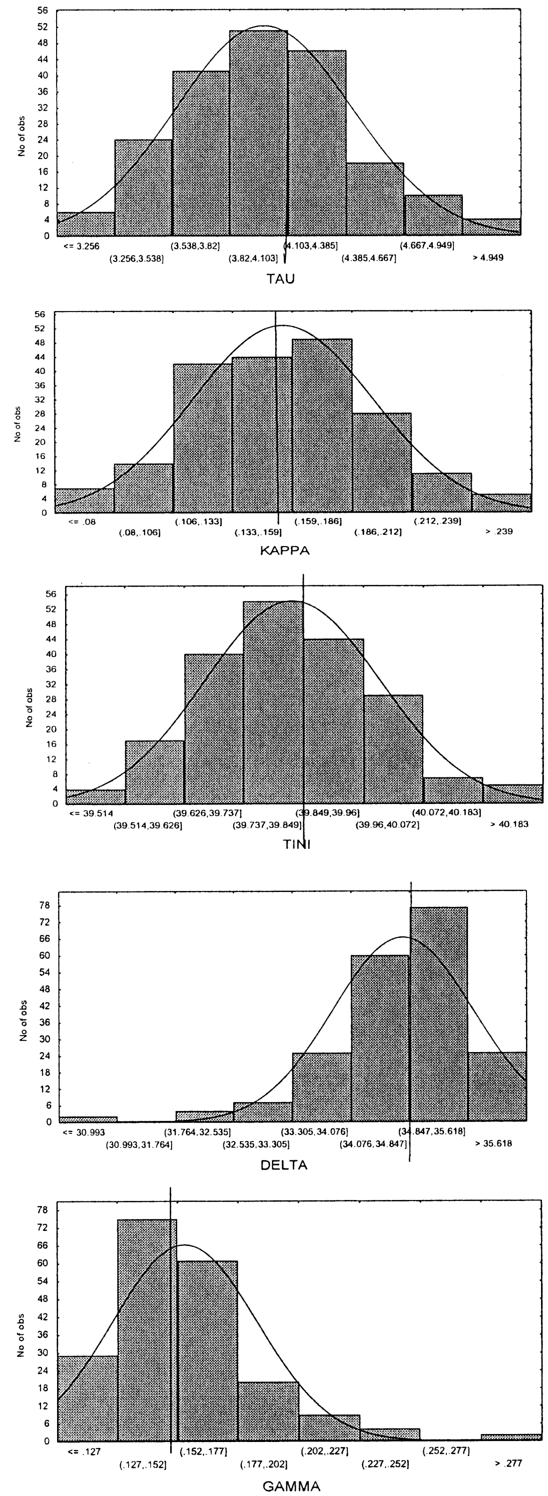

Table 8. SAS Code for Nlin Procedure

```
Proc Nlin Data=simulat outest=NLest Method=Marquardt hougaard Iter=500;
  Parms    kappa = &Kappa
           Tini  = &Tini
           delta = &delta
           gamma = &gamma;
  cosTH = Kappa /Sqrt(&omega**2 + Kappa**2) ;
  sinTH = &omega/Sqrt(&omega**2 + Kappa**2);
  temp1 = 1 /     (&omega**2 + kappa**2) ;
  theta = Atan(sinTH/cosTH);
  dTH_dk= -sinTH**2 / &omega;
       n=&omega;
 Model
  Tb   =  &mu*gamma + Delta
       + gamma*&amp*cosTH*(sin(&omega*(t- &phase))*cosTH - cos(&omega*(t-
         &phase))*sinTH)
       + (Kappa*gamma*(Kappa*&amp/(Kappa**2+&omega**2)*(sin(&omega*&phase)
       + &omega/Kappa*cos(&omega*&phase))-&mu/Kappa)
       + Tini-Delta)*exp(-Kappa*t);
der.kappa =
 gamma*(&amp*(-sinTH*( sin(n*(t-&phase))*cosTH  - cos(n*(t-&phase))*sinTH)
 +cosTH*(-sin(n*(t-&phase))*sinTH - cos(n*(t-&phase))*cosTH))*dTH_dk)
 +kappa*gamma*((kappa*&amp/(kappa**2+n**2)*
 (sin(n*&phase)+n/kappa*cos(n*&phase))-&mu/kappa)*(-t)*exp(-kappa*t)
 +(&amp*temp1**2*((n**2-kappa**2)*sin(n*&phase)-2*kappa*n*cos(n*&phase))
 +&mu/kappa**2)*exp(-kappa*t))
 +gamma*(kappa*&amp/(kappa**2+n**2)*(sin(n*&phase)+n/kappa*cos(n*&phase))
 -&mu/kappa)*exp(-kappa*t)
 +(Tini-Delta)*(-t)*exp(-kappa*t);

  der.Tini = exp(-kappa*t);
  der.Delta= 1-exp(-kappa*t);
  der.gamma =
    &mu + &amp*cosTH*(sin(n*(t-&phase))*cosTH -cos(n*(t-&phase))*sinTH)
    +kappa*(kappa*&amp/(kappa**2+n**2)*(sin(n*&phase)+n/kappa*cos(n*&phase))
    -&mu/kappa)*exp(-kappa*t);
  Output Out=B  P=Tbhat R=Tbresid;
Run;
```

Table 9. SAS Codes for Nlmixed Procedure

```
Proc Nlmixed Data=simulat COV CORR;

  Parms   kappa = &kappa
          Tini0  = &tini
          delta = &delta
          gamma = &gamma
          S2tb=0.002
          S2tini=0.1;
  bounds s2tb > 0, s2tini >0;
  n=&omega;
  cosTH = Kappa /Sqrt(&omega**2 + Kappa**2) ;
  sinTH = &omega/Sqrt(&omega**2 + Kappa**2);
  temp1 = 1 /     (&omega**2 + kappa**2) ;
  theta = Atan(sinTH/cosTH);
  dTH_dk= -sinTH**2 / &omega;
  n=&omega;
  Y  =  &mu*gamma + Delta
        + gamma*&amp*cosTH*(sin(&omega*(t- &phase))*cosTH - cos(&omega*(t-
          &phase))*sinTH)
        + (Kappa*gamma*(Kappa*&amp/(Kappa**2+&omega**2)*(sin(&omega*&phase)
        + &omega/Kappa*cos(&omega*&phase))-&mu/Kappa)
        + Tini-Delta)*exp(-Kappa*t);
  Model
        Tb ~ normal (y,s2tb);
  random tini ~ normal (tini0, s2tini) subject=steer;
  predict Tb  Out=B ;
  estimate "theta" Atan(n/kappa)/n;
 Run;
```