Human Liver		Male Mouse Liver		Female Mouse Liver
VVIAL	0.0119573	VVIAL	0.0119573	VVIAL
VMED	0.001	VMED	0.001	VMED
VINJ	0.0004	VINJ	0.0003858	VINJ
VAIR	VVIAL-VMED	VAIR	VVIAL-VMED	VAIR
P1	0.69	P1	0.69	P1
PROT	1	PROT	1	PROT

Human Lung		Male Mouse Lung		Female Mouse Lung
VVIAL	0.0119573	VVIAL	0.0119573	VVIAL
VMED	0.001	VMED	0.001	VMED
VINJ	0.0004	VINJ	0.0003858	VINJ
VAIR	VVIAL-VMED	VAIR	VVIAL-VMED	VAIR
P1	0.69	P1	0.69	P1
PROT	1	PROT	1	PROT

Male Mouse Kidney		Female Mouse Kidney		Male Rat Kidney
VVIAL	0.01163	VVIAL	0.01163	VVIAL
VMED	0.001	VMED	0.001	VMED
VINJ	0.0002	VINJ	0.0002	VINJ
VAIR	VVIAL-VMED	VAIR	VVIAL-VMED	VAIR
P1	0.69	P1	0.69	P1
PROT	2	PROT	2	PROT

	Male Rat Liver			Female Rat Liver	
0.01165	VVIAL	0.0119573		VVIAL	0.01165
0.001	VMED	0.001		VMED	0.001
0.0002	VINJ	0.0003858		VINJ	0.0002
VVIAL-VMED	VAIR	VVIAL-VMED		VAIR	VVIAL-VMED
0.69	P1	0.69		P1	0.69
1	PROT	1		PROT	1

	Male Rat Lung		Yang Rounded no reason given	Female Rat Lung	
0.01165	VVIAL	0.0119573	**0.012**	VVIAL	0.01165
0.001	VMED	0.001	**0.001**	VMED	0.001
0.0002	VINJ	0.0003858	**0.00039**	VINJ	0.0002
VVIAL-VMED	VAIR	VVIAL-VMED		VAIR	VVIAL-VMED
0.69	P1	0.69	**0.69**	P1	0.69
1	PROT	1	**1**	PROT	1

	Female Rat Kidney	
0.01163	VVIAL	0.01163
0.001	VMED	0.001
0.0002	VINJ	0.0002
VVIAL-VMED	VAIR	VVIAL-VMED
0.69	P1	0.69
3	PROT	3

Log

Female

		Median	95% CI	
Vmax	**µmol/hr/mg protein**	-2.25	-2.45	-2.07
Km	**µmol/L**	-0.80	-1.20	-0.43

Male

		Median	95% CI	
A0_1	**(umole)**	-1.4011	-1.5533	-1.2748
A0_2	**(umole)**	-2.1662	-2.3413	-2.0441
A0_3	**(umole)**	-3.0364	-3.158	-2.9356
A0_4	**(umole)**	-4.0041	-4.1409	-3.8725
A0_5	**(umole)**	-5.4951	-5.6864	-5.2974
Vmax	**µmol/hr/mg protein**	-1.5534	-1.8267	-1.3606
Km	**µmol/L**	-0.3732	-0.7498	-0.1023

EXP

Female

		Median	95% CI	
Vmax	**µmol/hr/mg protein**	0.105	0.087	0.127
Km	**µmol/L**	0.448	0.302	0.652

Male

		Median	95% CI	
A0_1	**(umole)**	0.25	0.21	0.28
A0_2	**(umole)**	0.11	0.10	0.13
A0_3	**(umole)**	0.048	0.043	0.053
A0_4	**(umole)**	0.018	0.016	0.021
A0_5	**(umole)**	0.0041	0.0034	0.0050
Vmax	**µmol/hr/mg protein**	0.212	0.161	0.257
Km	**µmol/L**	0.689	0.472	0.903

Female

```
> gelman.diag(x, autoburnin=FALSE)
Potential scale reduction

                Point est.
LI                      1          1
Vmax                    1          1
Km                      1          1

Multivariate psrf

             1
>
>            summary(x1)

Iterations   =          1:10000
Thinning     interval   =
Number       of         chains
Sample       size       per

             1 Empirical mean
               plus      standard

               Mean      SD
LI                0.463     0.0714
Vmax             -2.254     0.09479
Km               -0.804     0.19359

             2 Quantiles   for

                  2.50%      25%
LI               0.3484    0.4115
Vmax            -2.4452   -2.3159
Km               -1.197   -0.9271

>            summary(x2)

Iterations   =          1:10000
Thinning     interval   =
Number       of         chains
Sample       size       per

             1 Empirical mean
               plus      standard

               Mean      SD
LI               0.4648    0.07197
Vmax             -2.255    0.0946
```

factors:

Upper C.I.

1
= 1
chain = 10000

and standard deviation for each variable,
error of the mean:

Naive SE	Time-series SE	
0.000714	0.001377	
0.0009479	0.004866	4.2%
0.0019359	0.009858	24.1%

each variable:

50%	75%	97.50%
0.4552	0.5051	0.6204
-2.2542	-2.1914	-2.0651
-0.8026	-0.6756	-0.4282

1
= 1
chain = 10000

and standard deviation for each variable,
error of the mean:

Naive SE	Time-series SE
0.0007197	0.001336
0.000946	0.005313

Male Mouse Liver with A0 (initial mass in vial) estiamted as part of MCMC

KGL	**0.22**

```
>                gelman.diag(x,
Potential        scale

                 Point
A0_1                      1.02
A0_2                      1.02
A0_3                      1.01
A0_4                         1
A0_5                         1
LI                           1
Vmax                      1.03
Km                        1.03

Multivariate     psrf

          1.02
>
>                summary(x1)

Iterations       =
Thinning         interval
Number           of
Sample           size

               1 Empirical
                 plus

                 Mean
A0_1                   -1.4031
A0_2                   -2.1699
A0_3                   -3.0399
A0_4                   -4.0048
A0_5                   -5.4939
LI                      0.2548
Vmax                   -1.5577
Km                      -0.379

               2 Quantiles

                      2.50%
A0_1                -1.5533
A0_2                -2.3413
A0_3                 -3.158
A0_4                -4.1409
```

L/hr

autoburnin=FALSE)
reduction factors:

est.	Upper C.I.
1.07	
1.07	
1.03	
1	
1	
1	
1.09	
1.08	

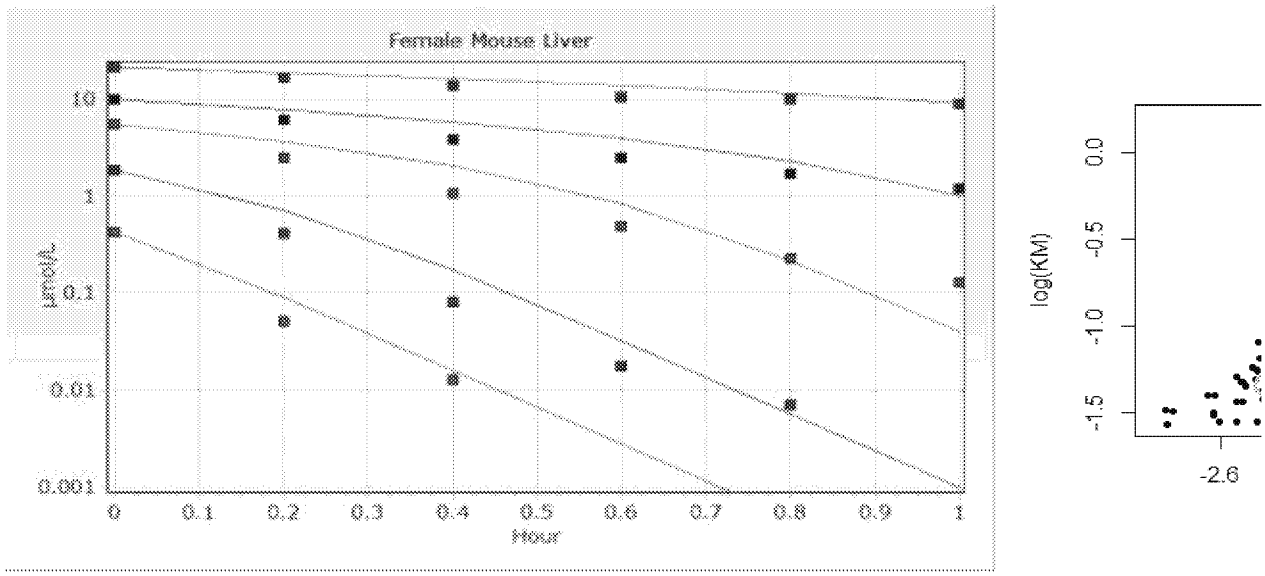
1:10000
= 1
chains = 1
per chain = 10000

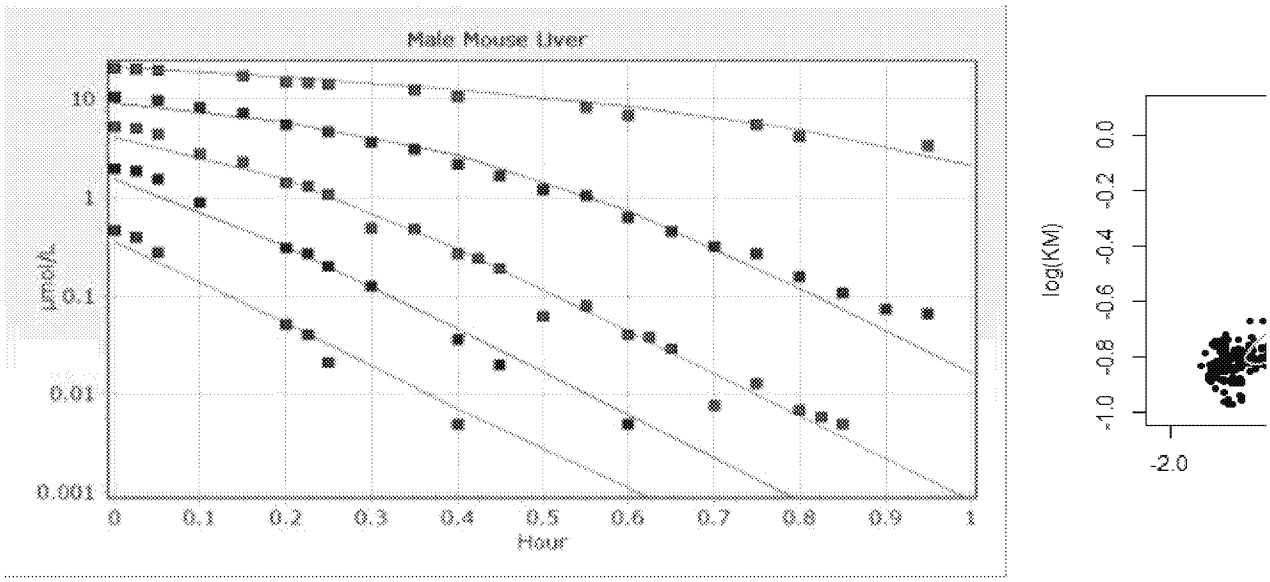
mean and standard deviation for each variable,
standard error of the mean:

SD	Naive SE	Time-series SE
0.06879	0.0006879	0.0107408
0.07131	0.0007131	0.0118313
0.05659	0.0005659	0.0048489
0.06784	0.0006784	0.0019284
0.09902	0.0009902	0.0026424
0.02239	0.0002239	0.0005144
0.10895	0.0010895	0.0222747
0.14721	0.0014721	0.0242133

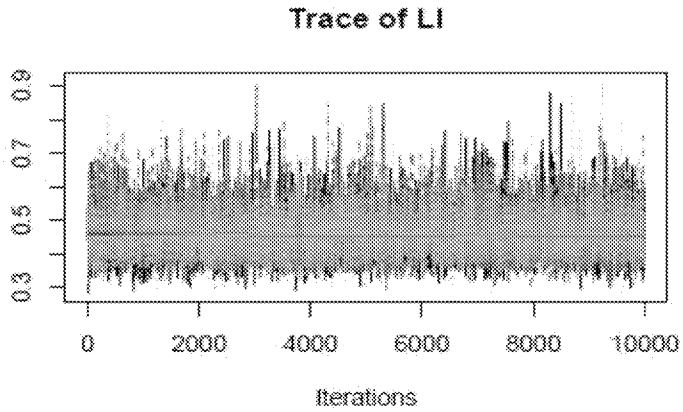
for each variable:

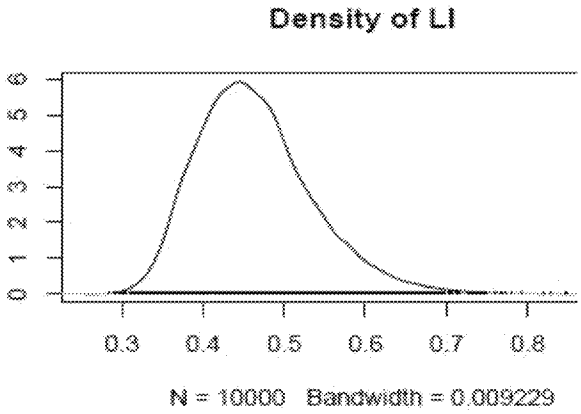
25%	50%	75%	97.50%
-1.4453	-1.4011	-1.357	-1.2748
-2.2097	-2.1662	-2.1227	-2.0441
-3.0749	-3.0364	-3.0014	-2.9356
-4.0501	-4.0041	-3.9599	-3.8725



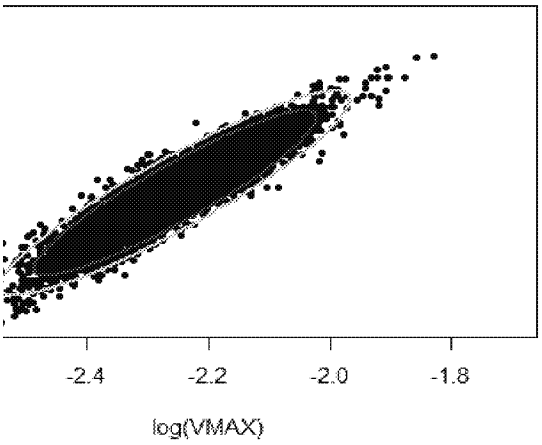


Female Mouse

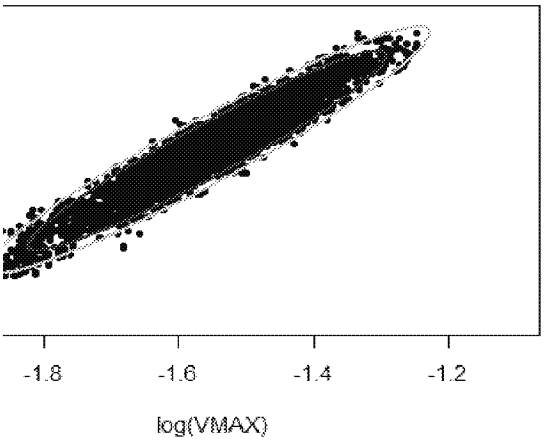




Female Mouse Liver

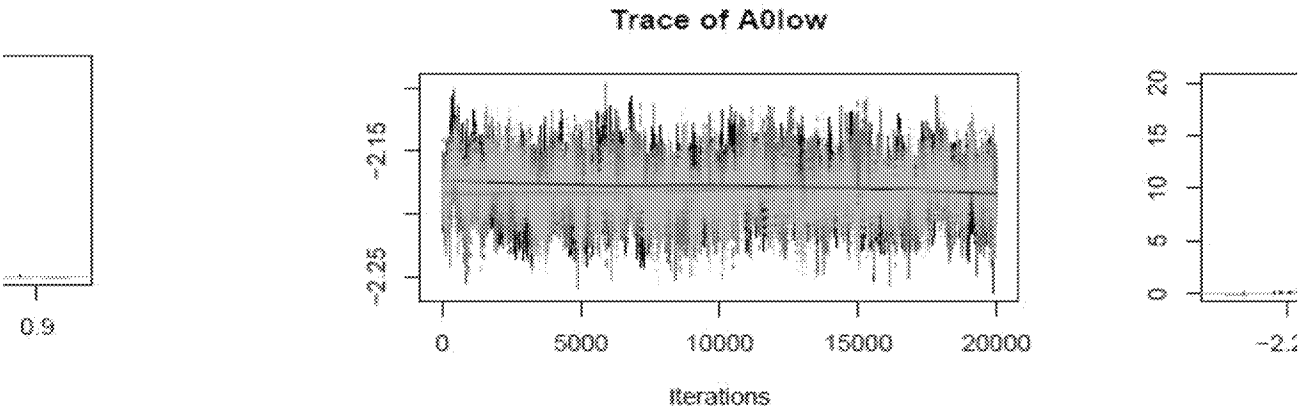


Male Mouse Liver




```
Km                    -0.8064          0.19593

          2 Quantiles        for

                   2.50%              25%
LI                0.3498           0.4155
Vmax             -2.4456          -2.3141
Km                  -1.2          -0.9323

>         summary(x3)

Iterations     =          1:10000
Thinning       interval   =
Number         of         chains
Sample         size       per

          1 Empirical     mean
            plus          standard

            Mean          SD
LI              0.4654          0.07343
Vmax           -2.2523          0.10187
Km             -0.8004          0.20872

          2 Quantiles        for

                   2.50%              25%
LI                0.351           0.4128
Vmax             -2.443          -2.3192
Km               -1.196          -0.9347
```

Male Mouse



0.0019593 0.010827

each variable:

50%	75%	97.50%
0.4559	0.5039	0.6313
-2.2558	-2.1937	-2.0711
-0.8038	-0.6782	-0.4217

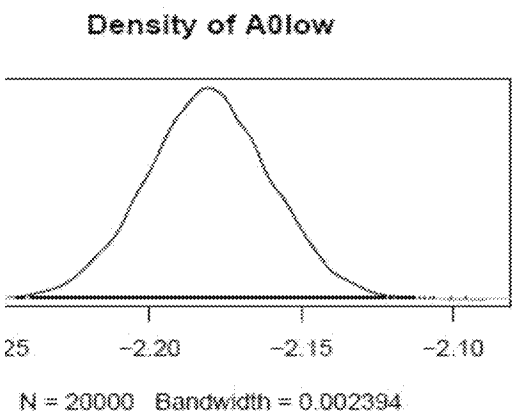
1
= 1
chain = 10000

and standard deviation for each variable,
error of the mean:

Naive SE	Time-series SE
0.0007343	0.001407
0.0010187	0.005648
0.0020872	0.01159

each variable:

50%	75%	97.50%
0.4572	0.5053	0.6375
-2.2538	-2.1886	-2.0488
-0.801	-0.6742	-0.3819



```
A0_5                    -5.6864
LI                       0.2158
Vmax                    -1.8267
Km                      -0.7498

>               summary(x2)

Iterations      =
Thinning        interval
Number          of
Sample          size

                1 Empirical
                  plus

                  Mean
A0_1                    -1.4204
A0_2                    -2.1879
A0_3                    -3.0509
A0_4                    -4.0066
A0_5                    -5.4876
LI                       0.2544
Vmax                    -1.5867
Km                      -0.4147

                2 Quantiles

                         2.50%
A0_1                    -1.5481
A0_2                    -2.3234
A0_3                    -3.1609
A0_4                    -4.1363
A0_5                    -5.6823
LI                        0.215
Vmax                    -1.7887
Km                      -0.6893

>               summary(x3)

Iterations      =
Thinning        interval
Number          of
Sample          size

                1 Empirical
                  plus
```

-5.5615	-5.4951	-5.4269	-5.2974
0.2391	0.2533	0.2684	0.3033
-1.6164	-1.5534	-1.4872	-1.3606
-0.4606	-0.3732	-0.2838	-0.1023

1:10000
= 1
chains = 1
per chain = 10000

mean and standard deviation for each variable,
standard error of the mean:

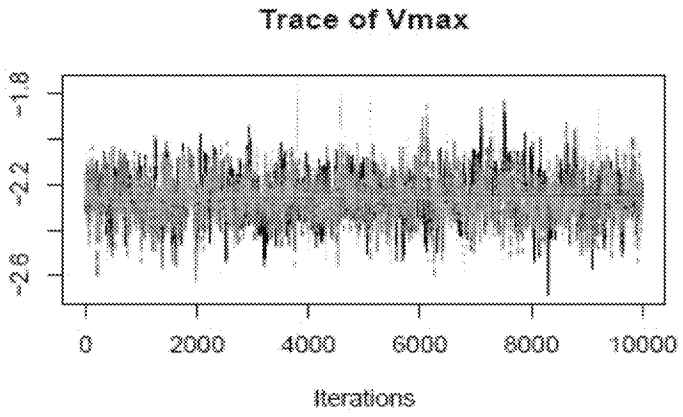
SD	Naive SE	Time-series SE
0.06697	0.0006697	0.0112243
0.07104	0.0007104	0.0106081
0.05793	0.0005793	0.004601
0.06586	0.0006586	0.0019443
0.09841	0.0009841	0.0023643
0.02243	0.0002243	0.0003978
0.10464	0.0010464	0.0203603
0.13689	0.0013689	0.0212758

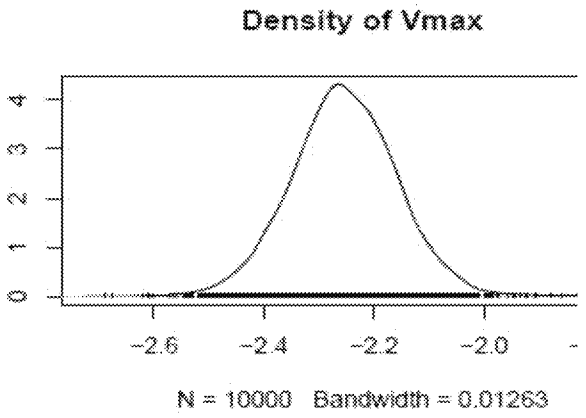
for each variable:

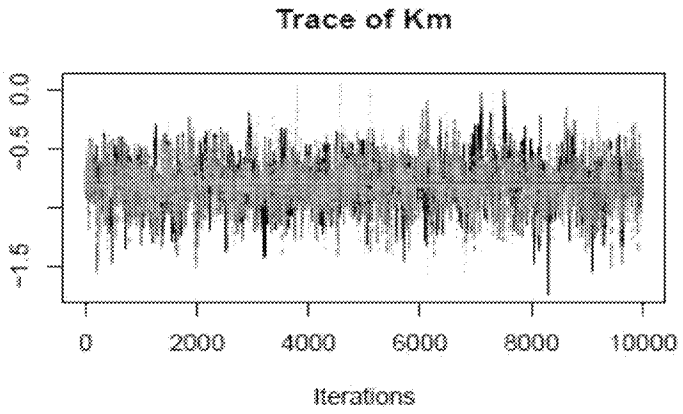
25%	50%	75%	97.50%
-1.4658	-1.4225	-1.3765	-1.2819
-2.237	-2.1894	-2.1402	-2.0409
-3.0916	-3.0503	-3.0113	-2.934
-4.0501	-4.0063	-3.9618	-3.8782
-5.5527	-5.4872	-5.4208	-5.2985
0.2386	0.2528	0.2693	0.3014
-1.656	-1.5906	-1.5222	-1.3627
-0.4984	-0.4177	-0.3338	-0.126

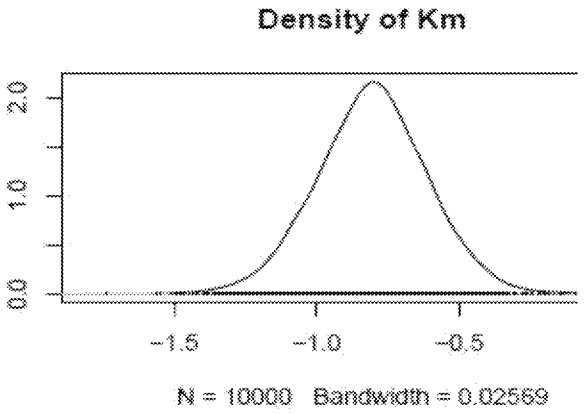
1:10000
= 1
chains = 1
per chain = 10000

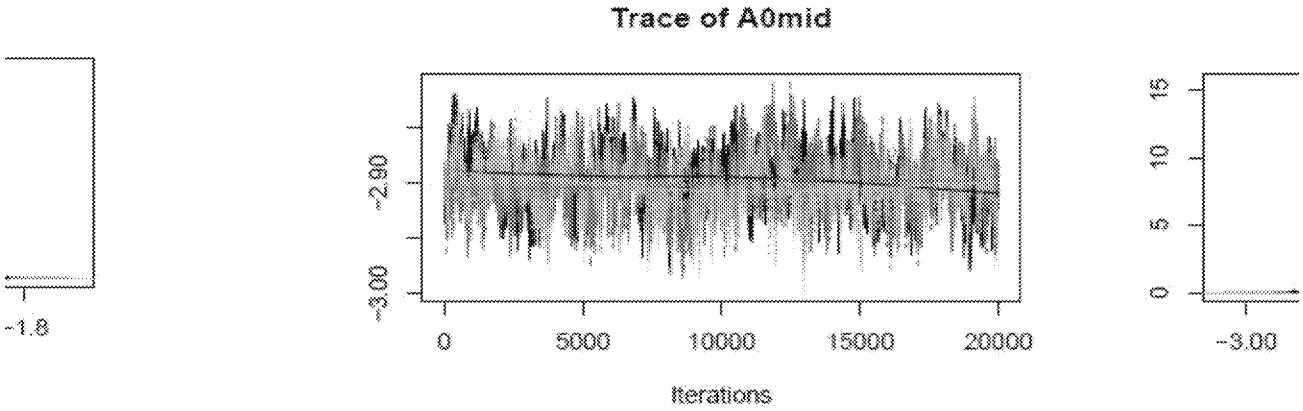
mean and standard deviation for each variable,
standard error of the mean:

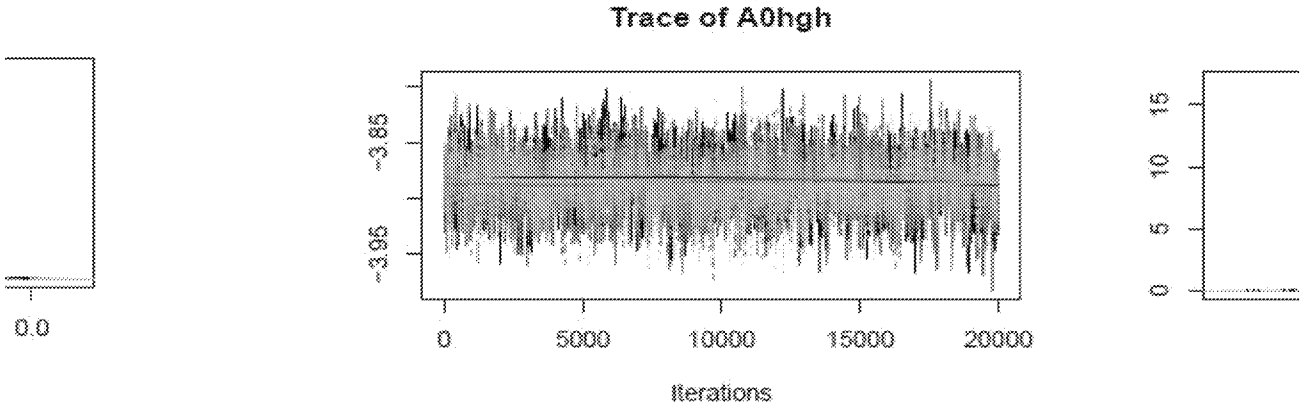

Trace of Vmax
−1.8
−2.2
−2.6
0
2000
4000
6000
8000
10000
Iterations

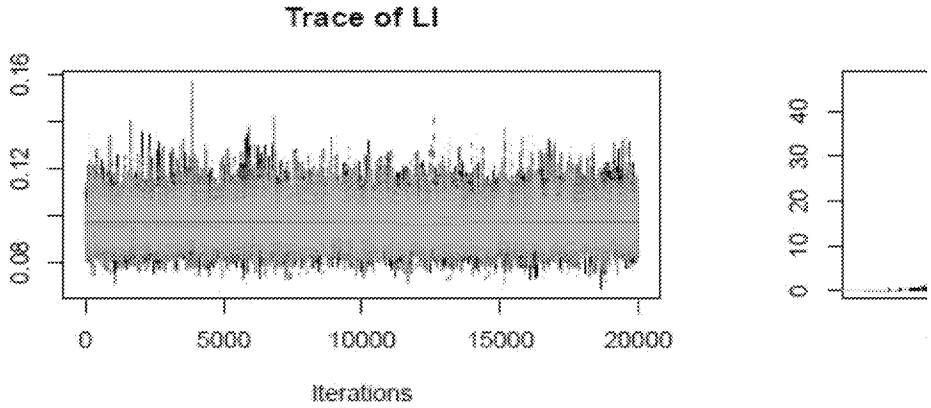

Density of Vmax
0
1
2
3
4
−2.6
−2.4
−2.2
−2.0
N = 10000 Bandwidth = 0.01263

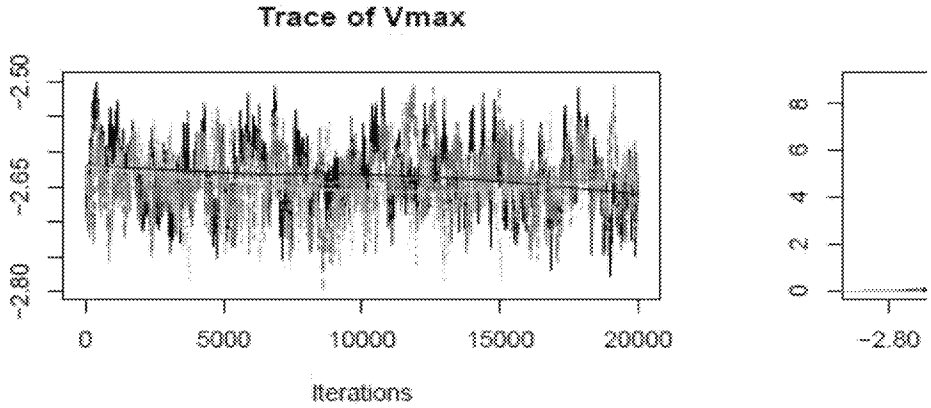

Trace of Km
0.0
−0.5
−1.5
0
2000
4000
6000
8000
10000
Iterations


Density of Km
0.0
1.0
2.0
−1.5
−1.0
−0.5
N = 10000 Bandwidth = 0.02569

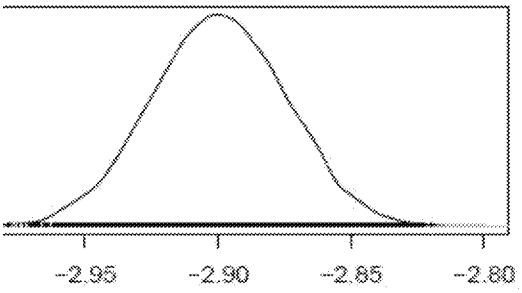

Trace of A0mid
-1.8
-2.90
-3.00
0
5000
10000
15000
20000
Iterations
0
5
10
15
-3.00


Trace of A0hgh
0.0
-3.85
-3.95
0
5000
10000
15000
20000
Iterations
0
5
10
15


Trace of LI
0.16
0.12
0.08
0
5000
10000
15000
20000
Iterations
0
10
20
30
40

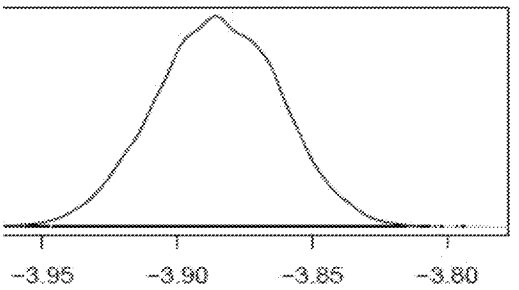

Trace of Vmax
-2.50
-2.65
-2.80
0
5000
10000
15000
20000
Iterations
0
2
4
6
8
-2.80

Density of A0mid



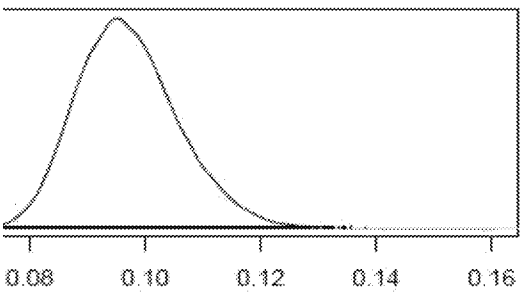
N = 20000 Bandwidth = 0.002946

Density of A0hgh



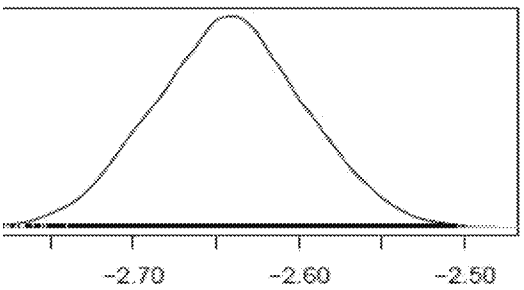
N = 20000 Bandwidth = 0.002722

Density of LI



N = 20000 Bandwidth = 0.001021

Density of Vmax



N = 20000 Bandwidth = 0.005308

	Mean
A0_1	-1.4013
A0_2	-2.1674
A0_3	-3.0409
A0_4	-4.0073
A0_5	-5.495
LI	0.254
Vmax	-1.5519
Km	-0.3675

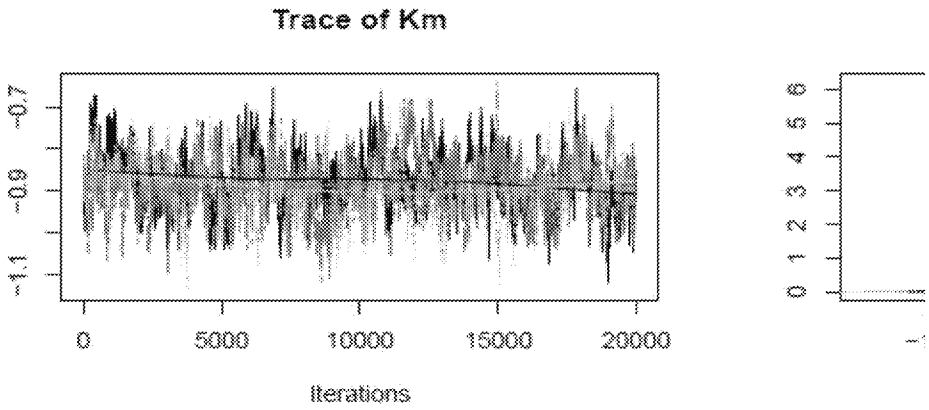
2 Quantiles

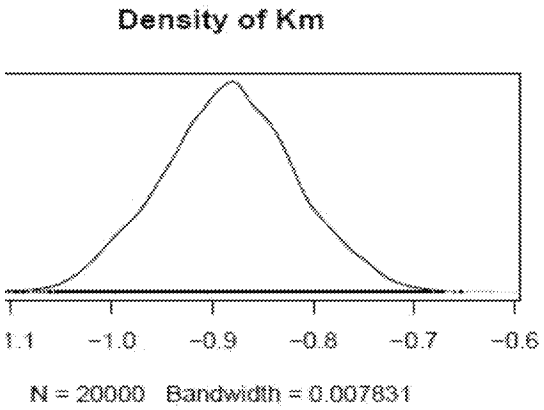
	2.50%
A0_1	-1.5239
A0_2	-2.2914
A0_3	-3.1469
A0_4	-4.1416
A0_5	-5.6897
LI	0.2145
Vmax	-1.7311
Km	-0.6231

SD	Naive	SE	Time-series	SE
0.06095	0.0006095	0.0076699		
0.06221	0.0006221	0.0086884		
0.05392	0.0005392	0.0040554		
0.06639	0.0006639	0.001816		
0.10034	0.0010034	0.002478		
0.02246	0.0002246	0.0004098		
0.09211	0.0009211	0.015206		
0.12389	0.0012389	0.0168887		

for each variable:

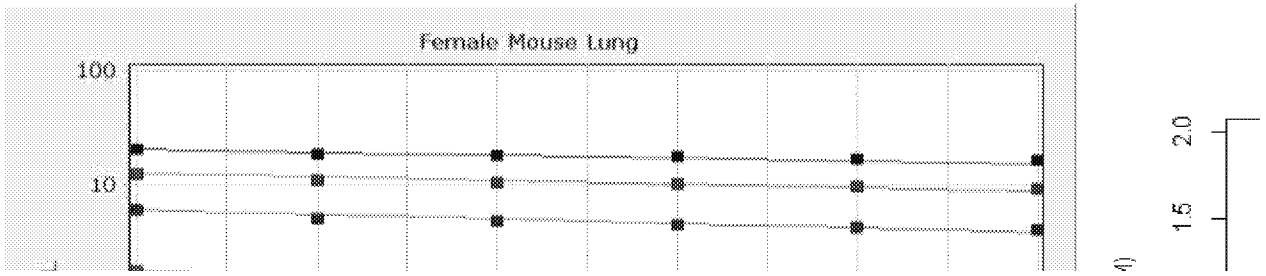
25%	50%	75%	97.50%
-1.4418	-1.3988	-1.3587	-1.2885
-2.209	-2.1661	-2.1237	-2.0542
-3.0767	-3.0413	-3.0052	-2.9345
-4.0508	-4.0072	-3.9617	-3.8783
-5.5619	-5.4949	-5.4279	-5.2964
0.2382	0.2528	0.2678	0.3014
-1.6151	-1.5468	-1.4864	-1.3898
-0.4485	-0.3621	-0.2771	-0.1494


Trace of Km
-0.7
-0.9
-1.1
0
5000
10000
15000
20000
Iterations
0 1 2 3 4 5 6


Density of Km
1.1
−1.0
−0.9
−0.8
−0.7
−0.6
N = 20000 Bandwidth = 0.007831

	Female				
			Median	**95% CI**	
Log	**Vmax**	**µmol/hr/mg protein**	-3.84	-4.20	-3.48
	Km	**µmol/L**	0.863	0.441	1.27
	Male				
			Median	**95% CI**	
	A0_1	**umol/L**	-0.012	-0.054	-0.00036
	A0_2	**umol/L**	-0.94	-1.00	-0.88
	A0_3	**umol/L**	-2.43	-2.52	-2.35
	A0_4	**umol/L**	-4.03	-4.10	-3.96
	A0_5	**umol/L**	-5.64	-5.74	-5.55
	Vmax	**µmol/hr/mg protein**	-2.47	-2.67	-2.25
	Km	**µmol/L**	0.177	-0.059	0.420

	Female				
			Median	**95% CI**	
EXP	**Vmax**	**µmol/hr/mg protein**	0.022	0.015	0.031
	Km	**µmol/L**	2.369	1.555	3.549
	Male				
			Median	**95% CI**	
	A0_1	**umol/L**	0.988	0.947	1.000
	A0_2	**umol/L**	0.391	0.367	0.414
	A0_3	**umol/L**	0.088	0.081	0.095
	A0_4	**umol/L**	0.018	0.017	0.019
	A0_5	**umol/L**	0.0035	0.0032	0.0039
	Vmax	**µmol/hr/mg protein**	0.085	0.069	0.105
	Km	**µmol/L**	1.194	0.943	1.523



Female > gelman.diag(x,
Potential scale

Point
LI 1
Vmax 1.01
Km 1.01

Multivariate psrf

1.01
>
> summary(x1)

Iterations =
Thinning interval
Number of
Sample size

1 Empirical
plus

Mean
LI 0.0579
Vmax -3.842
Km 0.8581

2 Quantiles

2.50%
LI 0.04563
Vmax -4.20138
Km 0.44118

> summary(x2)

Iterations =
Thinning interval
Number of
Sample size

1 Empirical
plus

Mean
LI 0.05808

Female Mouse Lung

autoburnin=FALSE)
reduction factors:

est.	Upper C.I.
1	
1.05	
1.04	

1:10000
= 1
chains = 1
per chain = 10000

mean and standard deviation for each variable,
standard error of the mean:

SD	Naive SE	Time-series SE
0.007529	7.53E-05	0.0001303
0.184502	1.85E-03	0.0158414 4.8%
0.213718	2.14E-03	0.0185756 24.9%

for each variable:

25%	50%	75%	97.50%
0.0525	0.05717	0.0624	0.07491
-3.9696	-3.83749	-3.7181	-3.47993
0.7097	0.86264	1.0014	1.2666

1:10000
= 1
chains = 1
per chain = 10000

mean and standard deviation for each variable,
standard error of the mean:

SD	Naive SE	Time-series SE
0.007425	7.43E-05	0.0001331

Male Mouse MCMC included estimation of the initial vial amount (A10)

Male	gelman.diag(x,
Potential	scale
	Point
A0_1	1
A0_2	1
A0_3	1
A0_4	1
A0_5	1
LI	1
Vmax	1
Km	1
Multivariate	psrf
	1
>	
>	summary(x1)
Iterations	=
Thinning	interval
Number	of
Sample	size
	1 Empirical
	plus
	Mean
A0_1	-0.01585
A0_2	-0.9402
A0_3	-2.43407
A0_4	-4.02598
A0_5	-5.64395
LI	0.12674
Vmax	-2.46803
Km	0.17784
	2 Quantiles
	2.50%
A0_1	-0.05397
A0_2	-1.00139
A0_3	-2.51684
A0_4	-4.09702
A0_5	-5.73964
LI	0.10695

autoburnin=FALSE)
reduction factors:

est.	Upper C.I.
1	
1	
1	
1	
1.01	
1	
1.01	
1.01	

1:10000 variable,
= 1
chains = 1
per chain = 10000

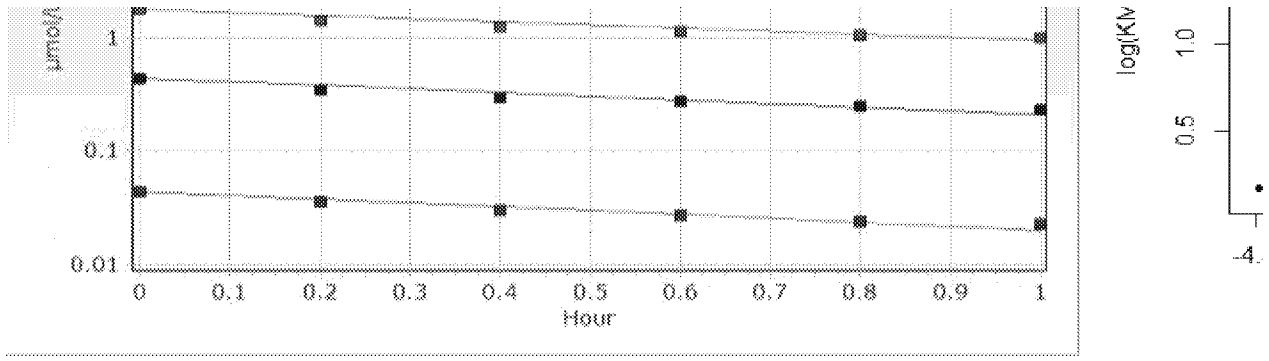
mean and standard deviation for each variable,
standard error of the mean:

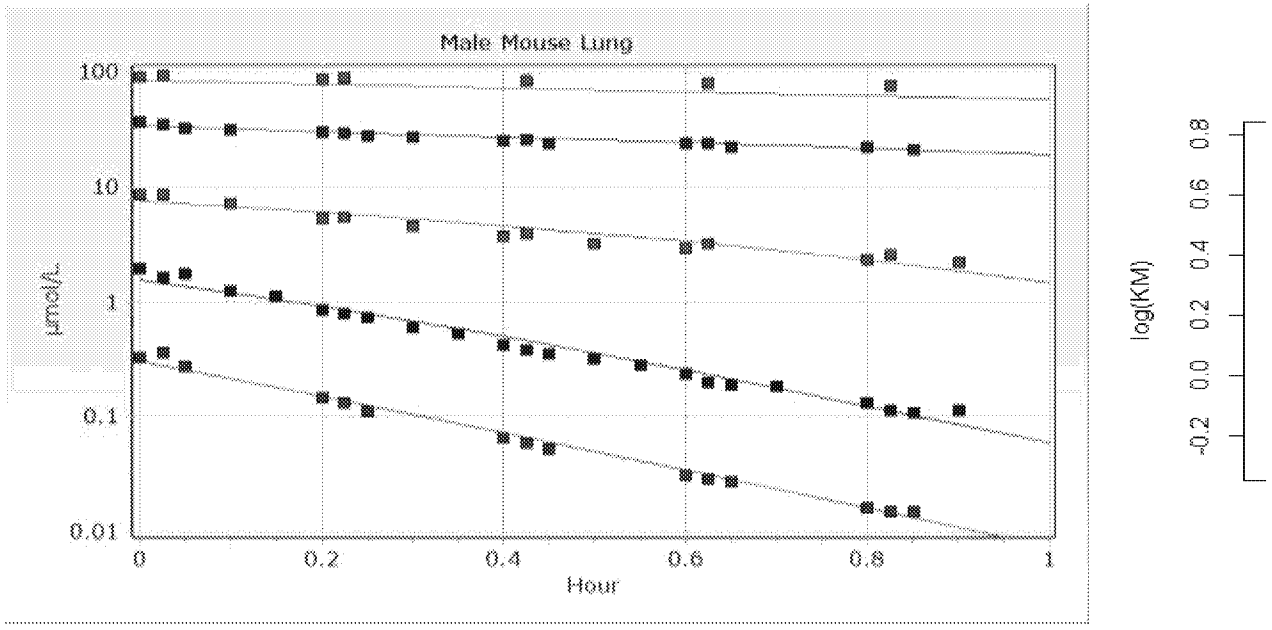
SD	Naive SE	Time-series SE
0.01458	0.0001458	0.0003125
0.03027	0.0003027	0.0011805
0.04258	0.0004258	0.0053045
0.03531	0.0003531	0.0016399
0.04792	0.0004792	0.001522
0.01109	0.0001109	0.0002005
0.1123	0.001123	0.0183254
0.12972	0.0012972	0.0205278

for each variable:

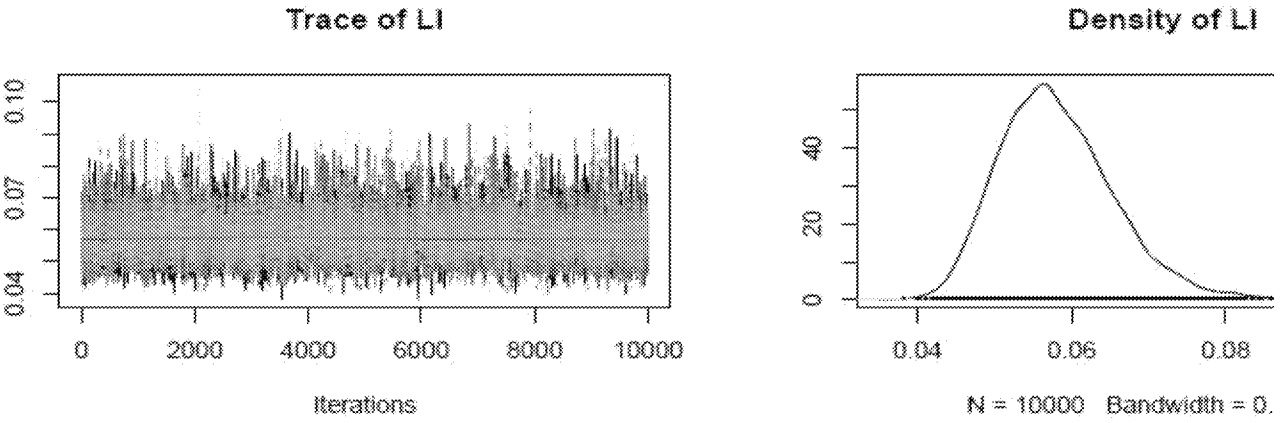
25%	50%	75%	97.50%
-0.02206	-0.01157	-0.00509	-0.0003616
-0.95979	-0.93976	-0.91986	-0.8818447
-2.46395	-2.43489	-2.40409	-2.352463
-4.04967	-4.02556	-4.00281	-3.9577505
-5.67606	-5.64298	-5.61096	-5.5503745
0.11919	0.12593	0.13359	0.1501522

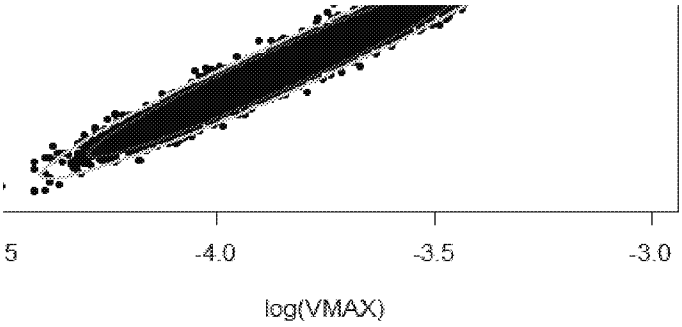
variable,





Female Mouse





Vmax	-3.87608
Km	0.81964

2 Quantiles

	2.50%
LI	0.0455
Vmax	-4.2715
Km	0.3694

> summary(x3)

Iterations =
Thinning interval
Number of
Sample size

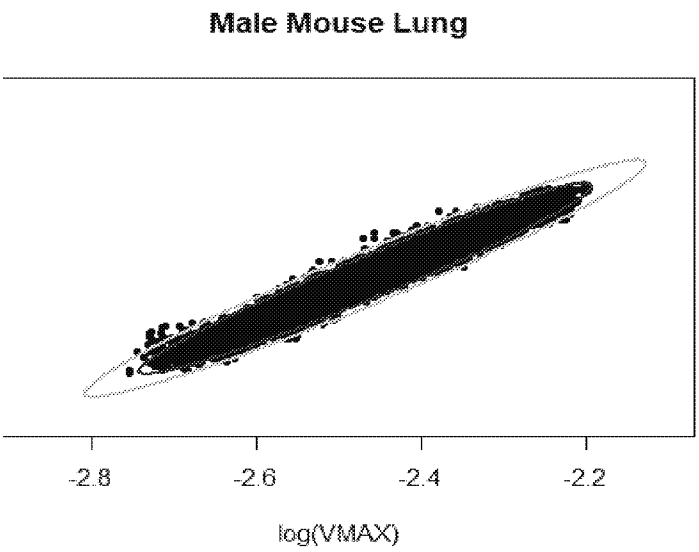
1 Empirical
plus

Mean

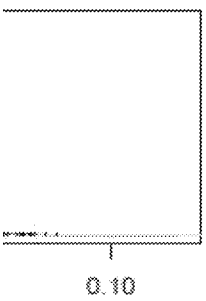
LI	0.05831
Vmax	-3.89248
Km	0.80088

2 Quantiles

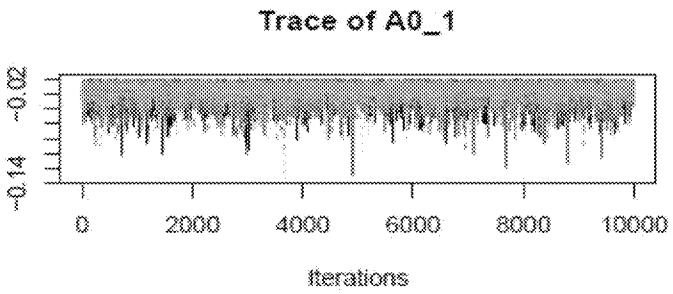
	2.50%
LI	0.04604
Vmax	-4.30746
Km	0.32312



Male Mouse



.000988



Trace of A0_2

0.185042	1.85E-03	0.0164477
0.215382	2.15E-03	0.0189728

for each variable:

25%	50%	75%	97.50%
0.0528	0.05733	0.06266	0.07436
-3.9843	-3.87417	-3.76142	-3.51551
0.6858	0.82193	0.95446	1.24341

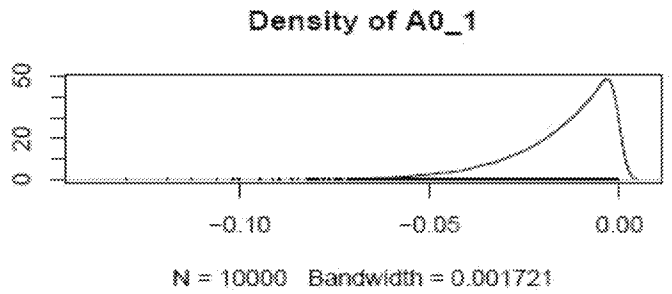
1:10000
= 1
chains = 1
per chain = 10000

mean and standard deviation for each variable,
standard error of the mean:

SD	Naive SE	Time-series SE
0.00742	0.0000742	0.0001423
0.19034	0.0019034	0.0170268
0.21932	0.0021932	0.0199335

for each variable:

25%	50%	75%	97.50%
0.053	0.05758	0.06264	0.07496
-4.01	-3.87513	-3.76253	-3.56032
0.6655	0.82077	0.95062	1.18926



Density of A0_2

```
Vmax                                    -2.67426
Km                                      -0.05884

>                                       summary(x2)

Iterations                              =
Thinning                                interval
Number                                  of
Sample                                  size

                                      1 Empirical
                                        plus

                                        Mean
A0_1                                    -0.01522
A0_2                                    -0.94095
A0_3                                    -2.43469
A0_4                                    -4.02509
A0_5                                    -5.63906
LI                                        0.127
Vmax                                     -2.4745
Km                                       0.16786

                                      2 Quantiles

                                          2.50%
A0_1                                    -0.05123
A0_2                                    -1.00219
A0_3                                    -2.51828
A0_4                                    -4.09717
A0_5                                    -5.73487
LI                                       0.10737
Vmax                                    -2.69554
Km                                       -0.0816

>                                       summary(x3)

Iterations                              =
Thinning                                interval
Number                                  of
Sample                                  size

                                      1 Empirical
                                        plus

                                        Mean
A0_1                                    -0.01499
```

-2.55349	-2.4688	-2.38657	-2.2546462
0.07594	0.17745	0.2748	0.4204822

1:10000
= 1
chains = 1
per chain = 10000

mean and standard deviation for each variable,
standard error of the mean:

SD	Naive SE	Time-series SE
0.01385	0.0001385	0.0002769
0.03085	0.0003085	0.00116
0.04286	0.0004286	0.0062176
0.03551	0.0003551	0.0017068
0.04804	0.0004804	0.0015741
0.01123	0.0001123	0.0002096
0.1139	0.001139	0.0201173
0.1316	0.001316	0.0214843

variable,

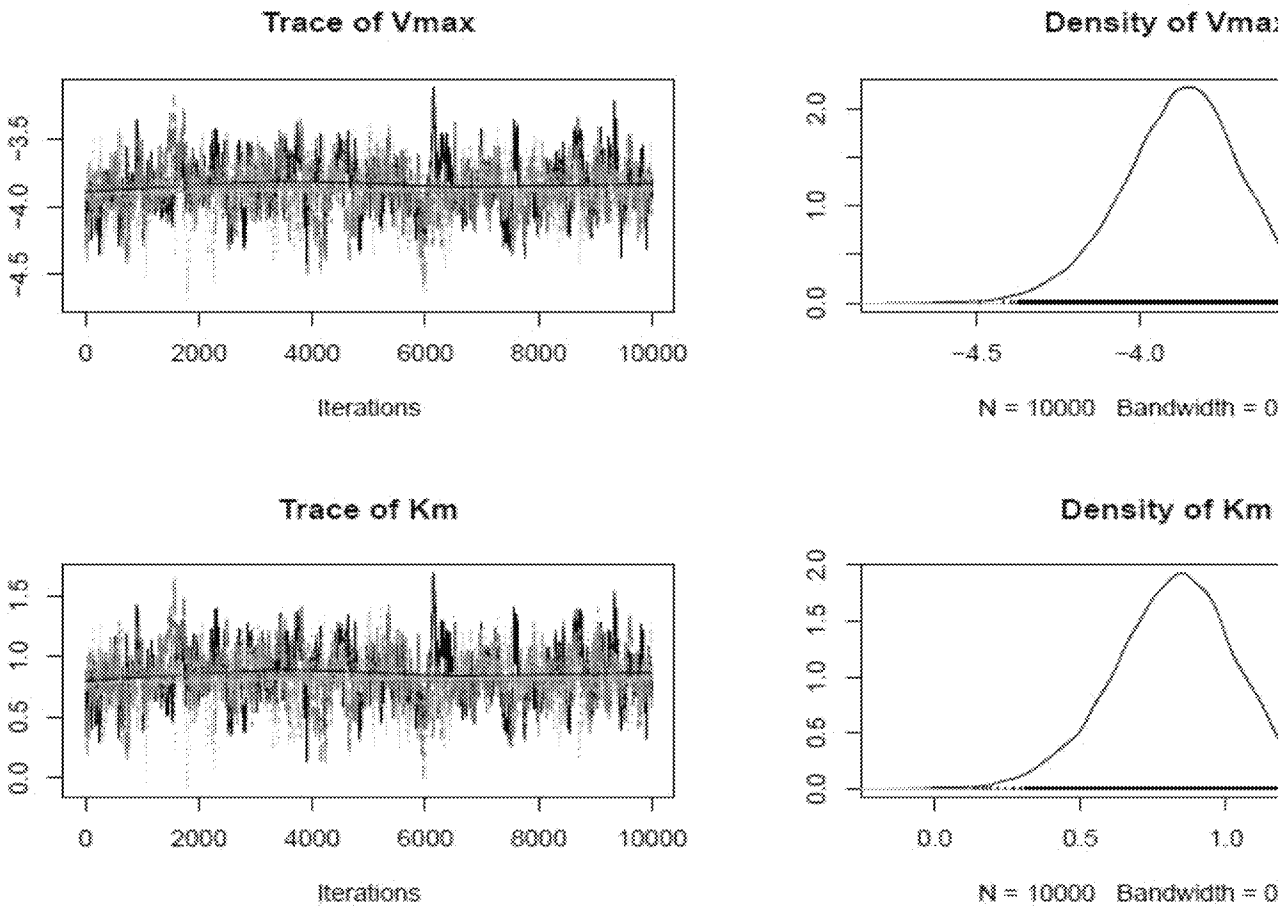
for each variable:

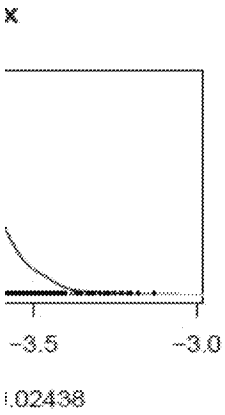
25%	50%	75%	97.50%
-0.02201	-0.01121	-0.004698	-0.0004468
-0.96156	-0.94071	-0.920617	-0.88009
-2.46179	-2.43581	-2.408952	-2.3436729
-4.04922	-4.02426	-4.001347	-3.9564021
-5.67024	-5.63913	-5.606319	-5.5466088
0.11903	0.12645	0.133848	0.1509449
-2.54648	-2.47714	-2.410262	-2.22794
0.08096	0.16372	0.24467	0.4550627

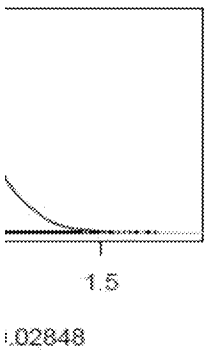
1:10000
= 1
chains = 1
per chain = 10000

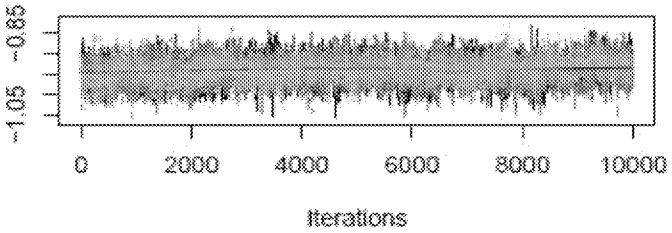
mean and standard deviation for each variable,
standard error of the mean:

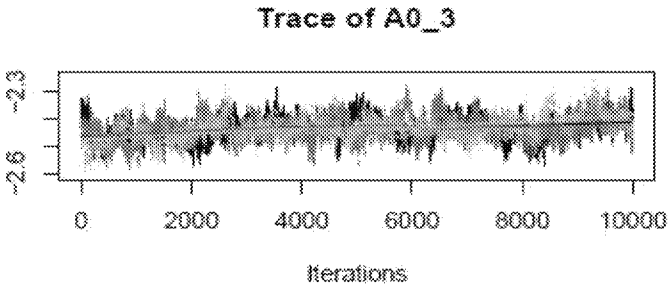
SD	Naive SE	Time-series SE
0.01376	0.0001376	0.0002704

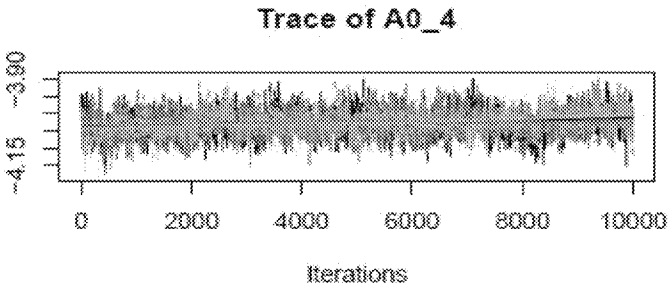

Trace of Vmax
Iterations
Density of Vma
N = 10000 Bandwidth = 0
Trace of Km
Iterations
Density of Km
N = 10000 Bandwidth = 0

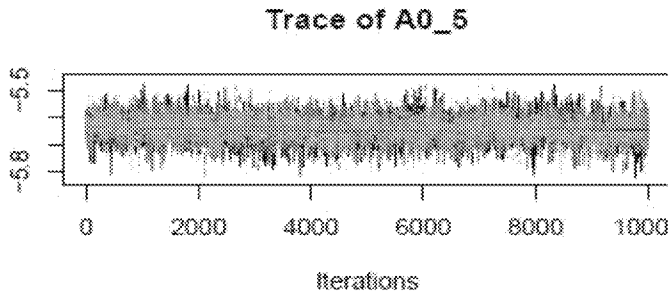

x
−3.5
−3.0
.02438

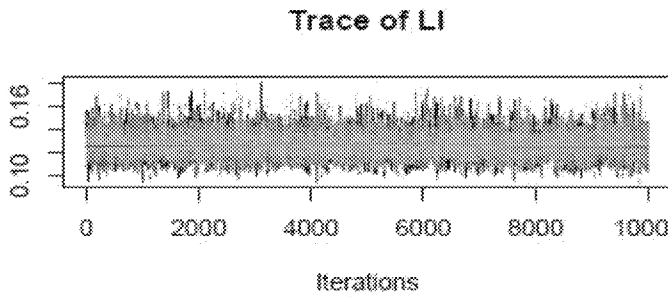

1.5
.02848

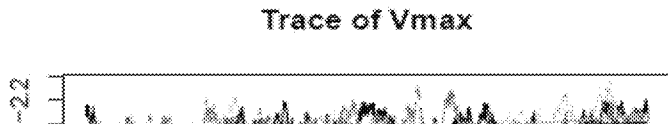

−0.85
−1.05
0
2000
4000
6000
8000
10000
Iterations

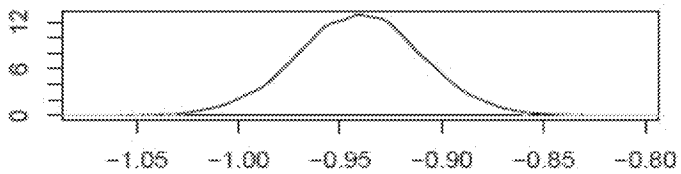

Trace of A0_3
−2.3
−2.6
0
2000
4000
6000
8000
10000
Iterations


Trace of A0_4
−3.90
−4.15
0
2000
4000
6000
8000
10000
Iterations


Trace of A0_5
−5.5
−5.8
0
2000
4000
6000
8000
1000
Iterations

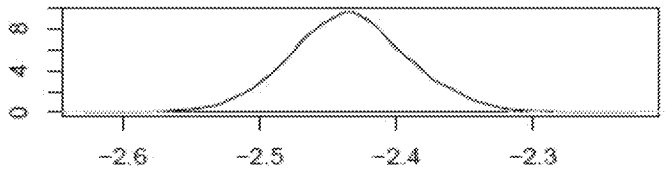

Trace of LI
0.16
0.10
0
2000
4000
6000
8000
1000
Iterations


Trace of Vmax
−2.2



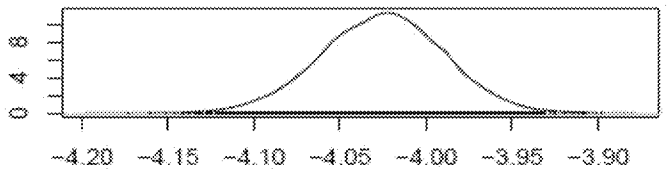
N = 10000 Bandwidth = 0.004104

Density of A0_3



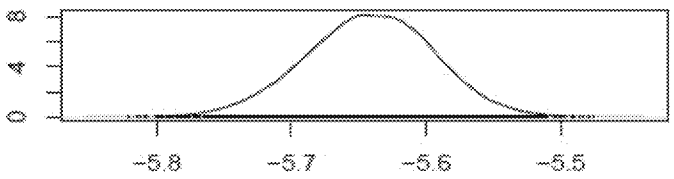
N = 10000 Bandwidth = 0.005736

Density of A0_4



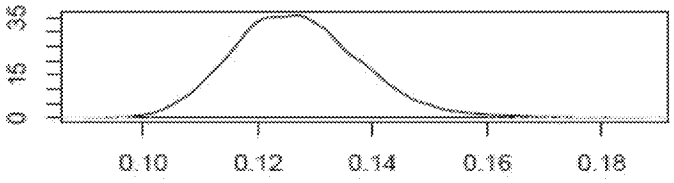
N = 10000 Bandwidth = 0.004835

Density of A0_5



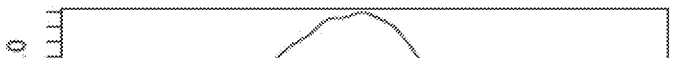
N = 10000 Bandwidth = 0.006498

Density of LI



N = 10000 Bandwidth = 0.001473

Density of Vmax



A0_2	-0.94057
A0_3	-2.43281
A0_4	-4.02546
A0_5	-5.64303
LI	0.12721
Vmax	-2.46624
Km	0.17945

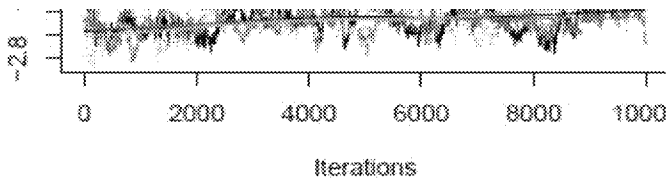
2 Quantiles

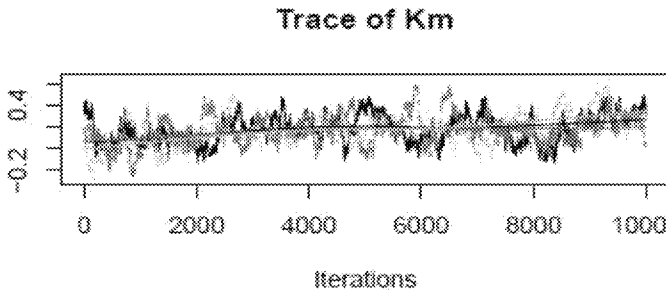
	2.50%
A0_1	-0.05018
A0_2	-1.00114
A0_3	-2.52399
A0_4	-4.09933
A0_5	-5.74106
LI	0.10714
Vmax	-2.72462
Km	-0.12116

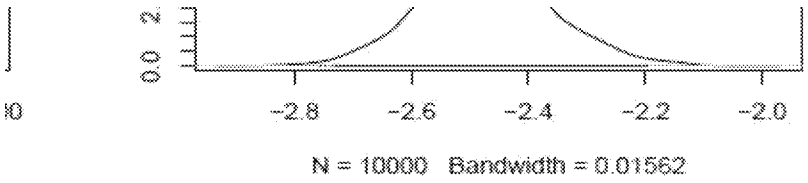
0.03139	0.0003139	0.0014902
0.04676	0.0004676	0.0078168
0.03717	0.0003717	0.0018356
0.04845	0.0004845	0.0015394
0.0113	0.000113	0.0002073
0.1282	0.001282	0.0240575
0.14681	0.0014681	0.0314077

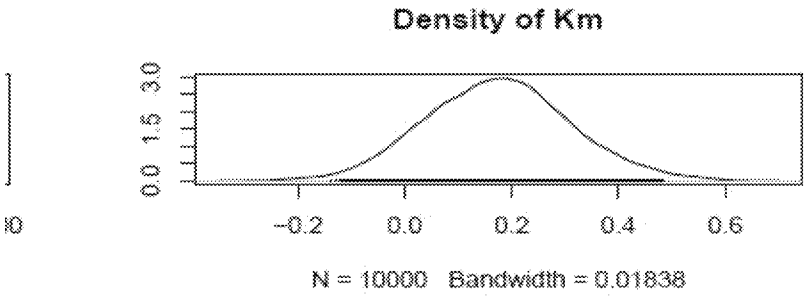
for each variable:

25%	50%	75%	97.50%
-0.02121	-0.011	-0.004497	-0.0004176
-0.96147	-0.9409	-0.920107	-0.8772421
-2.46298	-2.433	-2.404443	-2.336268
-4.04973	-4.0252	-4.000018	-3.952992
-5.67499	-5.6421	-5.609777	-5.551088
0.1193	0.1265	0.133989	0.1516964
-2.54743	-2.4616	-2.388776	-2.188453
0.08798	0.1842	0.269131	0.4902987


-2.8
0
2000
4000
6000
8000
1000
Iterations


Trace of Km
0.4
-0.2
0
2000
4000
6000
8000
1000
Iterations

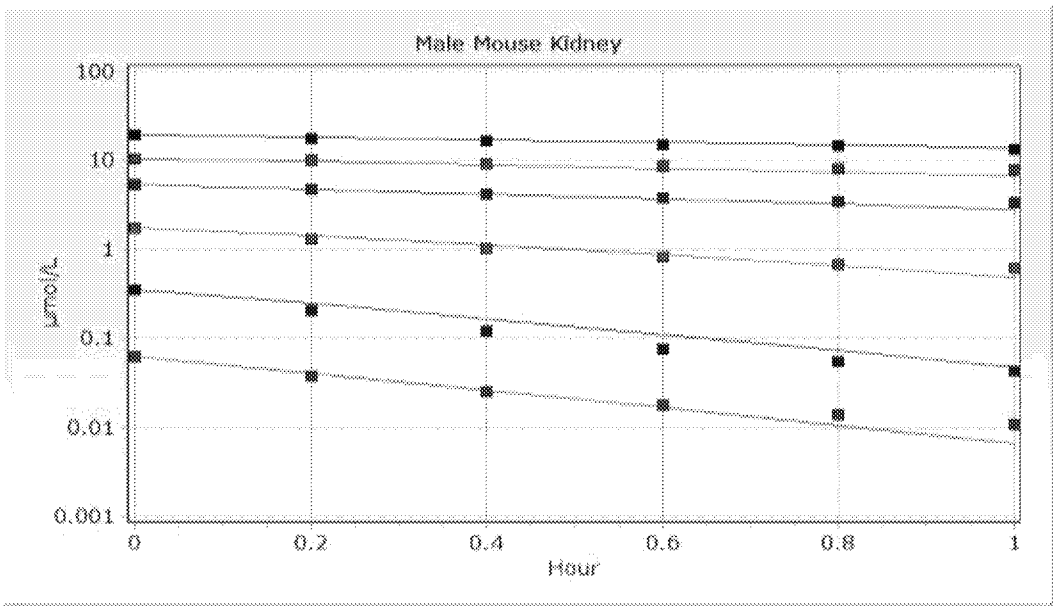

0.0
2
-2.8
-2.6
-2.4
-2.2
-2.0
N = 10000 Bandwidth = 0.01562


Density of Km
0.0
1.5
3.0
-0.2
0.0
0.2
0.4
0.6
N = 10000 Bandwidth = 0.01838

Log

Exp

ND - Female Mouse Kidney Figure - Indeterminate - data were insufficient to estimate in vitro metabolic parameters.



Female

not determinable - data were insufficient to estimate in vitro metabolic parameters.

Male

Vmax
Km

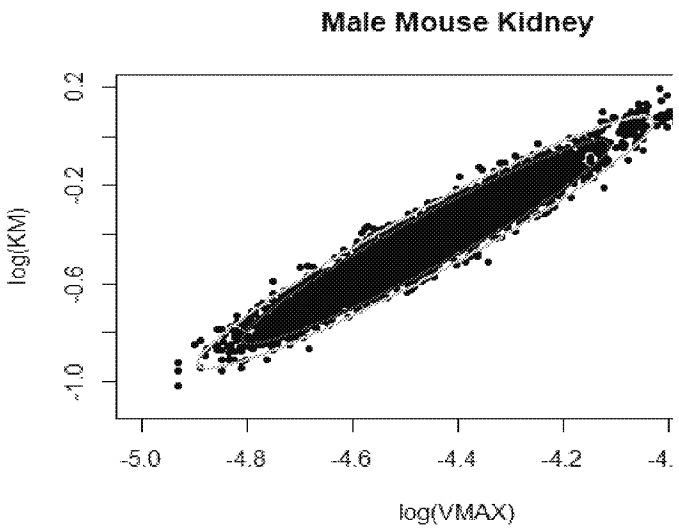
Male

Vmax
Km

	Median	95% CI	

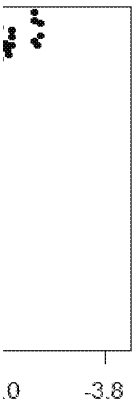
	Median	95% CI	
µmol/hr/mg protein	-4.46	-4.74	-4.18
µmol/L	-0.44	-0.76	-0.10

	Median	95% CI	
µmol/hr/mg protein	0.012	0.009	0.015
µmol/L	0.647	0.469	0.902



Female

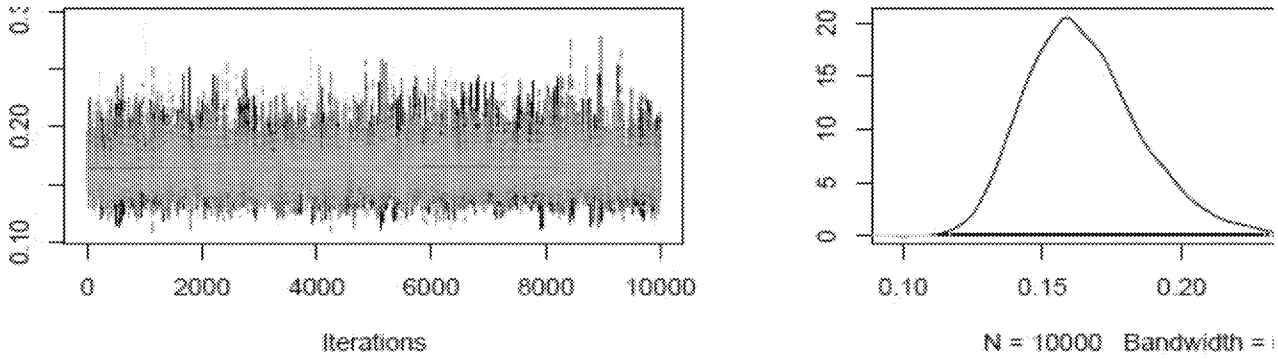
ND

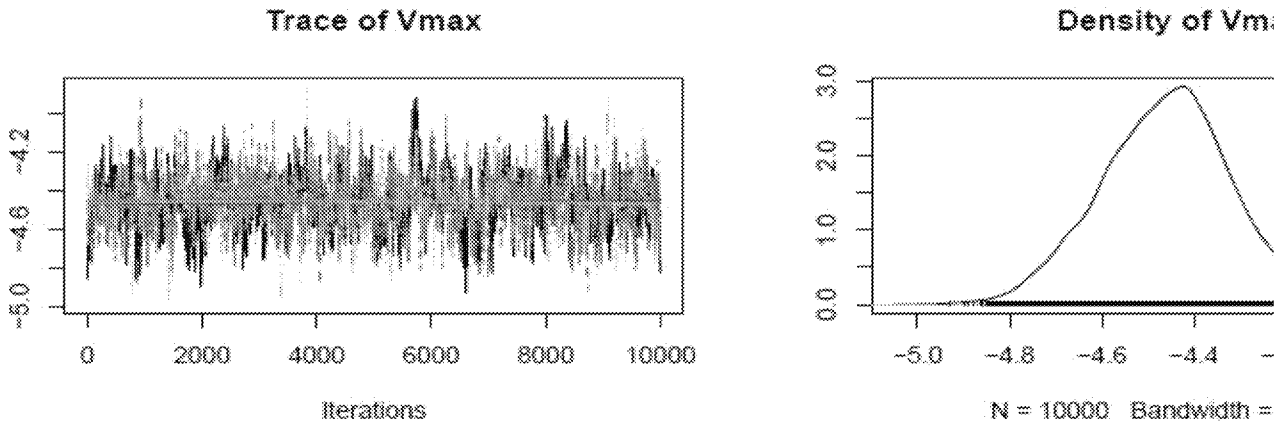


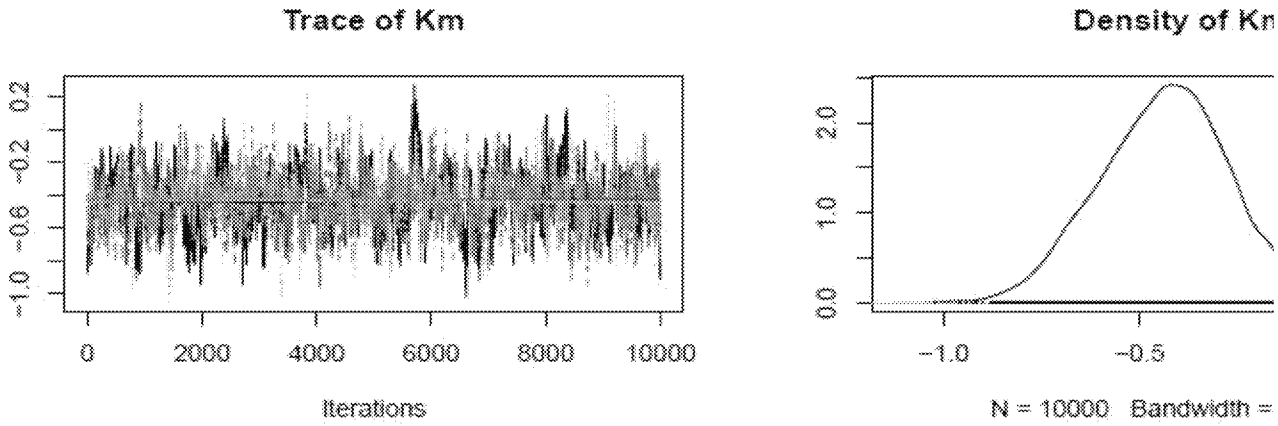
```
Male > gelman.diag(x, autoburnin=FALSE)
Potential scale reduction factors:

Point est. Upper C.I.
LI 1 1
Vmax 1 1.01
Km 1 1

Multivariate psrf

1
>
> summary(x1)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each
plus standard error of the mean:

Mean SD Naive SE Time-series SE
LI 0.1651 2.08E-02 2.08E-04 0.0003615
Vmax -4.4603 1.43E-01 1.43E-03 0.0104628
Km -0.4337 0.16994 0.0016994 0.0124705

2 Quantiles for each variable:

2.50% 25% 50% 75% 97.50%
LI 0.1303 1.50E-01 1.63E-01 0.1775 0.2118
Vmax -4.7366 -4.557 -4.4593 -4.365 -4.1838
Km -0.7573 -5.52E-01 -4.35E-01 -0.321 -0.1029

> summary(x2)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each
plus standard error of the mean:

Mean SD Naive SE Time-series SE
LI 0.1648 0.021 0.00021 0.0003713
Vmax -4.4546 0.1349 0.001349 0.009557
```

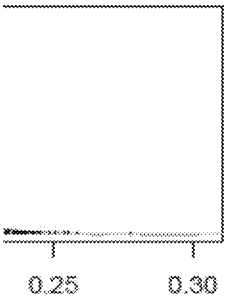
variable,

variable,


0.10
0.20
0
2000
4000
6000
8000
10000
Iterations
0
5
10
15
20
0.10
0.15
0.20
N = 10000 Bandwidth =

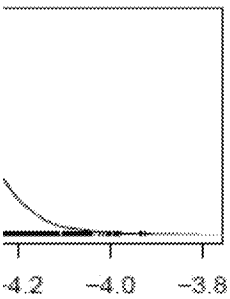

Trace of Vmax
−5.0
−4.8
−4.6
−4.4
0
2000
4000
6000
8000
10000
Iterations
Density of Vm
0.0
1.0
2.0
3.0
−5.0
−4.8
−4.6
−4.4
N = 10000 Bandwidth =


Trace of Km
−1.0
−0.6
−0.2
0.2
0
2000
4000
6000
8000
10000
Iterations
Density of Kn
0.0
1.0
2.0
−1.0
−0.5
N = 10000 Bandwidth =



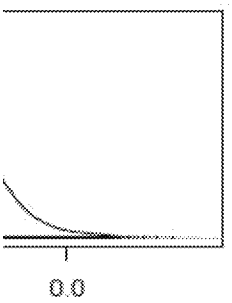
0.002725

ax



0.01896

n



0.02261

```
Km                    -0.4272              0.1611    0.001611  0.0111831

        2 Quantiles      for                 each      variable:

                    2.50%              25%       50%       75%      97.50%
LI                   0.13            0.1501    0.1623    0.1769      0.2123
Vmax                -4.729           -4.543   -4.4509   -4.3685     -4.1825
Km                  -0.747          -0.5326   -0.4239   -0.3237     -0.1012

>       summary(x3)

Iterations    =          1:10000
Thinning      interval   =                    1
Number        of         chains     =              1
Sample        size       per        chain      =          10000

        1 Empirical      mean       and        standard   deviation  for    each
          plus           standard   error      of         the        mean:

          Mean           SD         Naive      SE         Time-series SE
LI                0.1648          0.02117  0.0002117  0.0003731
Vmax             -4.4659          0.14904  0.0014904   0.012136
Km               -0.4392          0.17666  0.0017666  0.0142073

        2 Quantiles      for                 each      variable:

                    2.50%              25%       50%       75%      97.50%
LI                  0.1295           0.1501    0.1625    0.1772      0.2126
Vmax               -4.7654          -4.5655   -4.4579   -4.3666     -4.1832
Km                 -0.7861          -0.5577   -0.4305   -0.3206     -0.1111
```

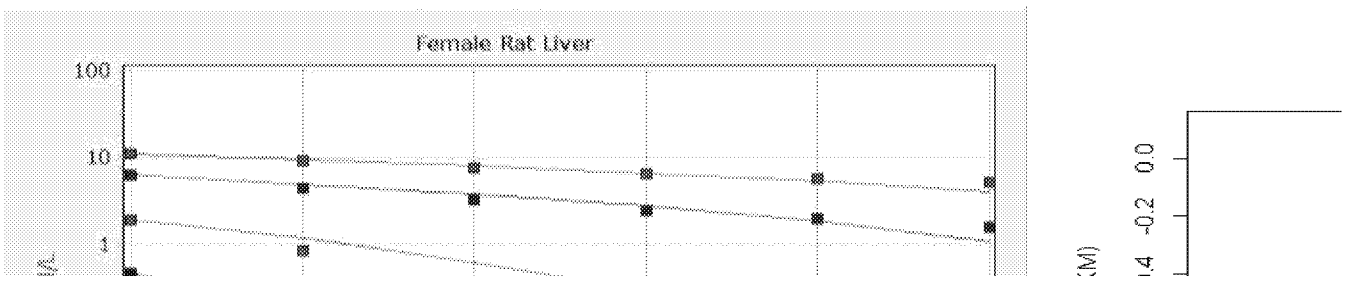
variable,

	Female				
			Median	**95% CI**	
Log	**Vmax**	**µmol/hr/mg protein**	-2.67	-2.89	-2.46
	Km	**µmol/L**	-0.33	-0.61	-0.07

Male				
		Median	**95% CI**	
A0low	**µmol**	-2.17842	-2.21784	-2.1387
A0mid	**µmol**	-2.89622	-2.94343	-2.8474
A0hgh	**µmol**	-3.88276	-3.92974	-3.8375
Vmax	**µmol/hr/mg protein**	-2.63578	-2.71817	-2.5459
Km	**µmol/L**	-0.87566	-1.00163	-0.7395

	Female				
			Median	**95% CI**	
EXP	**Vmax**	**µmol/hr/mg protein**	0.069	0.056	0.085
	Km	**µmol/L**	0.718	0.544	0.933

Male				
		Median	**95% CI**	
A0low	**µmol**	0.113	0.109	0.118
A0mid	**µmol**	0.055	0.053	0.058
A0hgh	**µmol**	0.021	0.020	0.022
Vmax	**µmol/hr/mg protein**	0.072	0.066	0.078
Km	**µmol/L**	0.417	0.367	0.477



Female > gelman.diag(x, autoburnin=FALSE)
Potential scale reduction factors:

	Point est.	Upper
LI	1	1
Vmax	1	1.01
Km	1	1.01

Multivariate psrf

1
>
> summary(x1)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain

1 Empirical mean and plus standard error

	Mean	SD	Naive
LI	0.3076	0.04605	0.0004605
Vmax	-2.6741	0.10833	0.0010833
Km	-0.3299	0.13802	0.0013802

2 Quantiles for each

	2.50%	25%	50%
LI	0.2342	0.2753	0.3028
Vmax	-2.8874	-2.7434	-2.6732
Km	-0.6087	-0.418	-0.3307

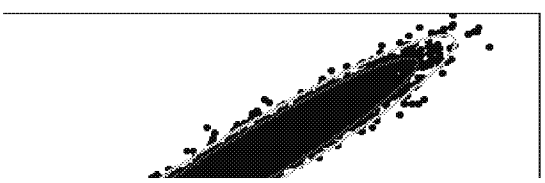
> summary(x2)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain

1 Empirical mean and plus standard error

	Mean	SD	Naive
LI	0.3065	0.04528	0.0004528
Vmax	-2.6785	0.10232	0.0010232

Female Rat Liver



Male gelman.diag(x, autoburnin=FALSE)

Potential scale reduction

C.I.

	Point	est.
A0low	1.01	1.02
A0mid	1.01	1.04
A0hgh	1.01	1.02
LI	1	1
Vmax	1.01	1.05
Km	1.01	1.04

Multivariate psrf

1.01

```
>
> summary(x1)
```

1

= 10000

Iterations = 1:20000

Thinning interval =

standard deviation for each variable,

Number of chains

Sample size per

SE Time-series SE

1 Empirical mean

plus standard

0.0009012

0.0070518

0.0090673

	Mean	SD
A0low	-2.17827	0.02023
A0mid	-2.89614	0.02463
A0hgh	-3.88286	0.02364
LI	0.09722	0.00884
Vmax	-2.63501	0.04433
Km	-0.87484	0.06706

variable:

2 Quantiles for

	2.50%	25%
A0low	-2.21784	-2.19193
A0mid	-2.94343	-2.91332
A0hgh	-3.92974	-3.89875
LI	0.08166	0.09098
Vmax	-2.71817	-2.66599
Km	-1.00163	-0.92033

75%	97.50%
0.3333	0.4141
-2.6016	-2.464
-0.2365	-0.0689

1

= 10000

standard deviation for each variable,

of the mean:

```
> summary(x2)
```

SE Time-series SE

0.0008561

0.0068566

Iterations = 1:20000

Thinning interval =

factors:

Upper C.I.

1
= 1
chain = 20000

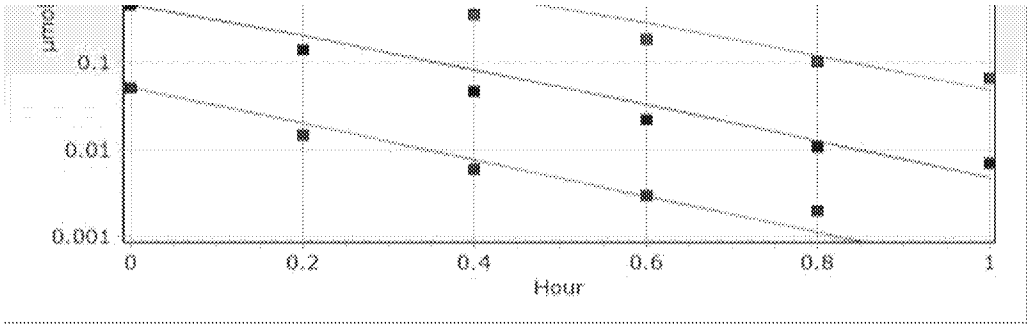
and standard deviation for each variable,
error of the mean:

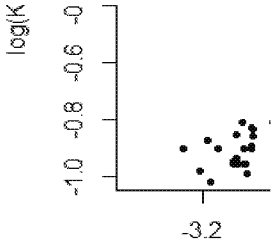
Naive SE	Time-series SE
1.43E-04	0.0011228
1.74E-04	0.0021708
1.67E-04	0.0008139
6.25E-05	0.0001176
3.14E-04	0.0045295
4.74E-04	0.0058892

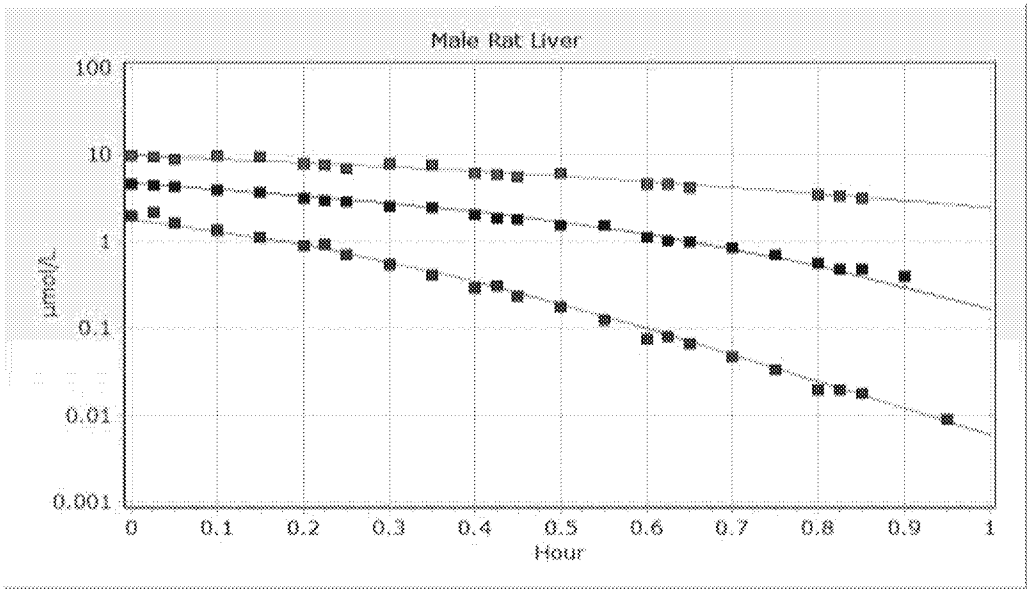
each variable:

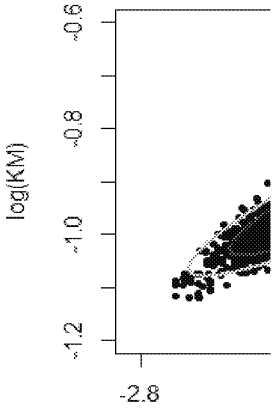
50%	75%	97.50%
-2.17842	-2.1647	-2.1387
-2.89622	-2.8789	-2.8474
-3.88276	-3.8663	-3.8375
0.09644	0.1027	0.1163
-2.63578	-2.605	-2.5459
-0.87566	-0.8312	-0.7395

1

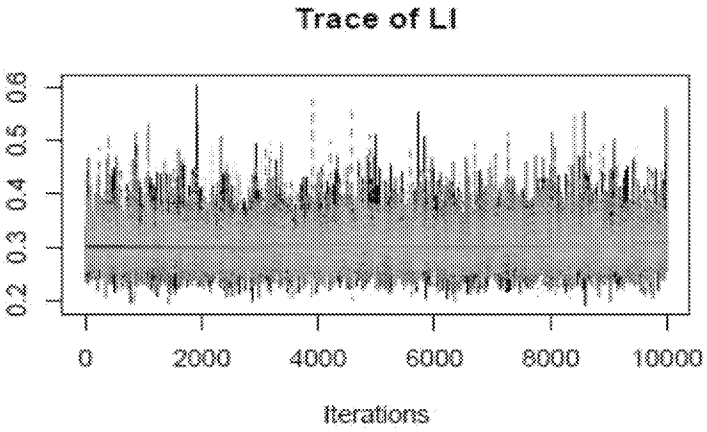

0.1
0.01
0.001
0
0.2
0.4
0.6
0.8
1
Hour

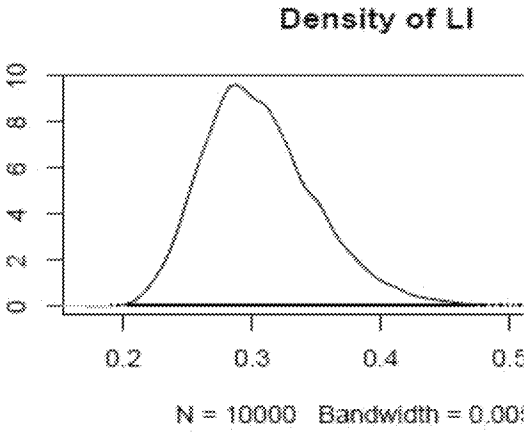

log(K
-0
-0.6
-0.8
-1.0
-3.2

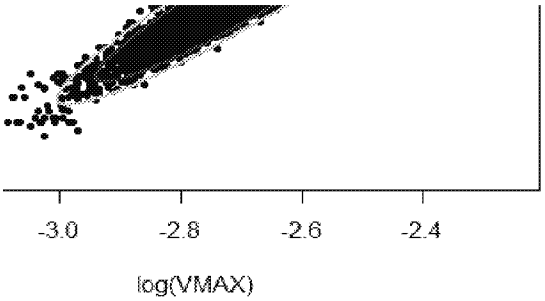

Male Rat Liver
100
10
1
0.1
0.01
0.001
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Hour


log(KM)
-0.6
-0.8
-1.0
-1.2
-2.8

Female Rat


Trace of LI
0.2
0.3
0.4
0.5
0.6
0
2000
4000
6000
8000
10000
Iterations


Density of LI
0
2
4
6
8
10
0.2
0.3
0.4
N = 10000 Bandwidth = 0.00



Km -0.3362 0.13038 0.0013038

2 Quantiles for each

	2.50%	25%	50%
LI	0.2331	0.2751	0.3003
Vmax	-2.8733	-2.7483	-2.6803
Km	-0.5844	-0.424	-0.3383

> summary(x3)

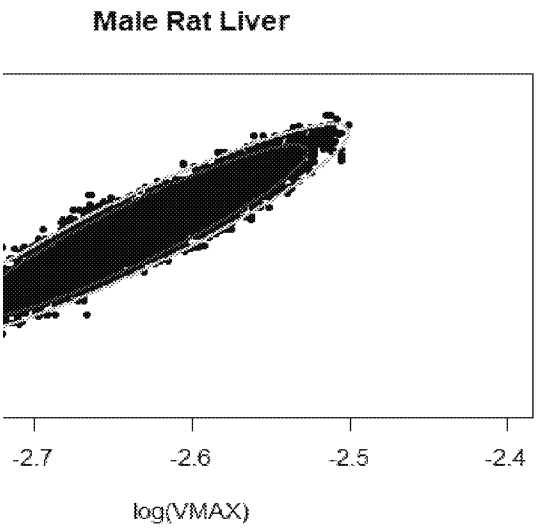
Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain

1 Empirical mean and plus standard error

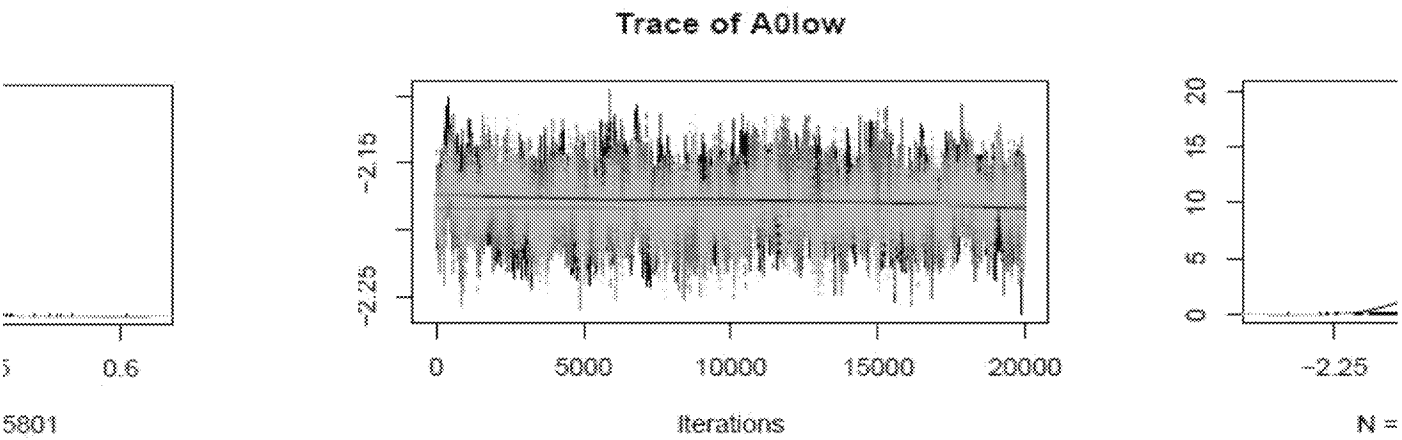
	Mean	SD	Naive
LI	0.3071	0.0436	0.000436
Vmax	-2.6687	0.1051	0.001051
Km	-0.3234	0.1356	0.001356

2 Quantiles for each

	2.50%	25%	50%
LI	0.2344	0.2754	0.3028
Vmax	-2.8753	-2.7405	-2.6674
Km	-0.5903	-0.4118	-0.3233



Male Rat



0.008862

variable:

75%	97.50%
0.3322	0.40887
-2.6109	-2.47317
-0.2543	-0.07111

1
= 10000

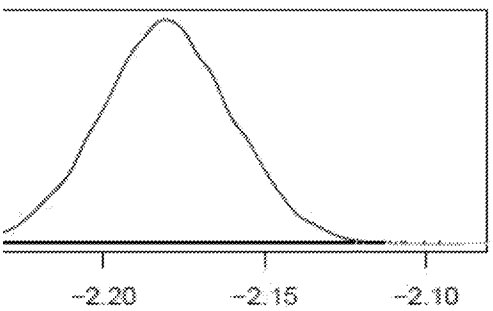
standard deviation for each variable,
of the mean:

SE Time-series SE
0.0008392
0.0068841
0.0088825

variable:

75%	97.50%
0.3334	0.40573
-2.5973	-2.4678
-0.2321	-0.06045

Density of A0low



20000 Bandwidth = 0.002394

Number of chains
Sample size per

1 Empirical mean
plus standard

	Mean	SD
A0low	-2.18124	0.020526
A0mid	-2.90017	0.025076
A0hgh	-3.88545	0.022686
LI	0.09712	0.008951
Vmax	-2.64286	0.045271
Km	-0.88512	0.067828

2 Quantiles for

	2.50%	25%
A0low	-2.22161	-2.19472
A0mid	-2.94867	-2.91746
A0hgh	-3.9307	-3.90064
LI	0.08162	0.09081
Vmax	-2.72777	-2.67353
Km	-1.01462	-0.9304

> summary(x3)

Iterations = 1:20000
Thinning interval =
Number of chains
Sample size per

1 Empirical mean
plus standard

	Mean	SD
A0low	-2.18215	0.020584
A0mid	-2.9029	0.025119
A0hgh	-3.88692	0.023042
LI	0.09704	0.008725
Vmax	-2.64807	0.045076
Km	-0.89208	0.067185

2 Quantiles for

	2.50%	25%
A0low	-2.2232	-2.19569
A0mid	-2.95412	-2.91937

= 1
chain = 20000

and standard deviation for each variable,
error of the mean:

Naive SE	Time-series SE
1.45E-04	0.0013599
1.77E-04	0.0021241
1.60E-04	0.0008748
6.33E-05	0.0001264
3.20E-04	0.0049098
4.80E-04	0.0068644

each variable:

50%	75%	97.50%
-2.18149	-2.1678	-2.1402
-2.90032	-2.8832	-2.8498
-3.88506	-3.8699	-3.8422
0.09656	0.1027	0.1164
-2.64321	-2.613	-2.5502
-0.88501	-0.8404	-0.7454

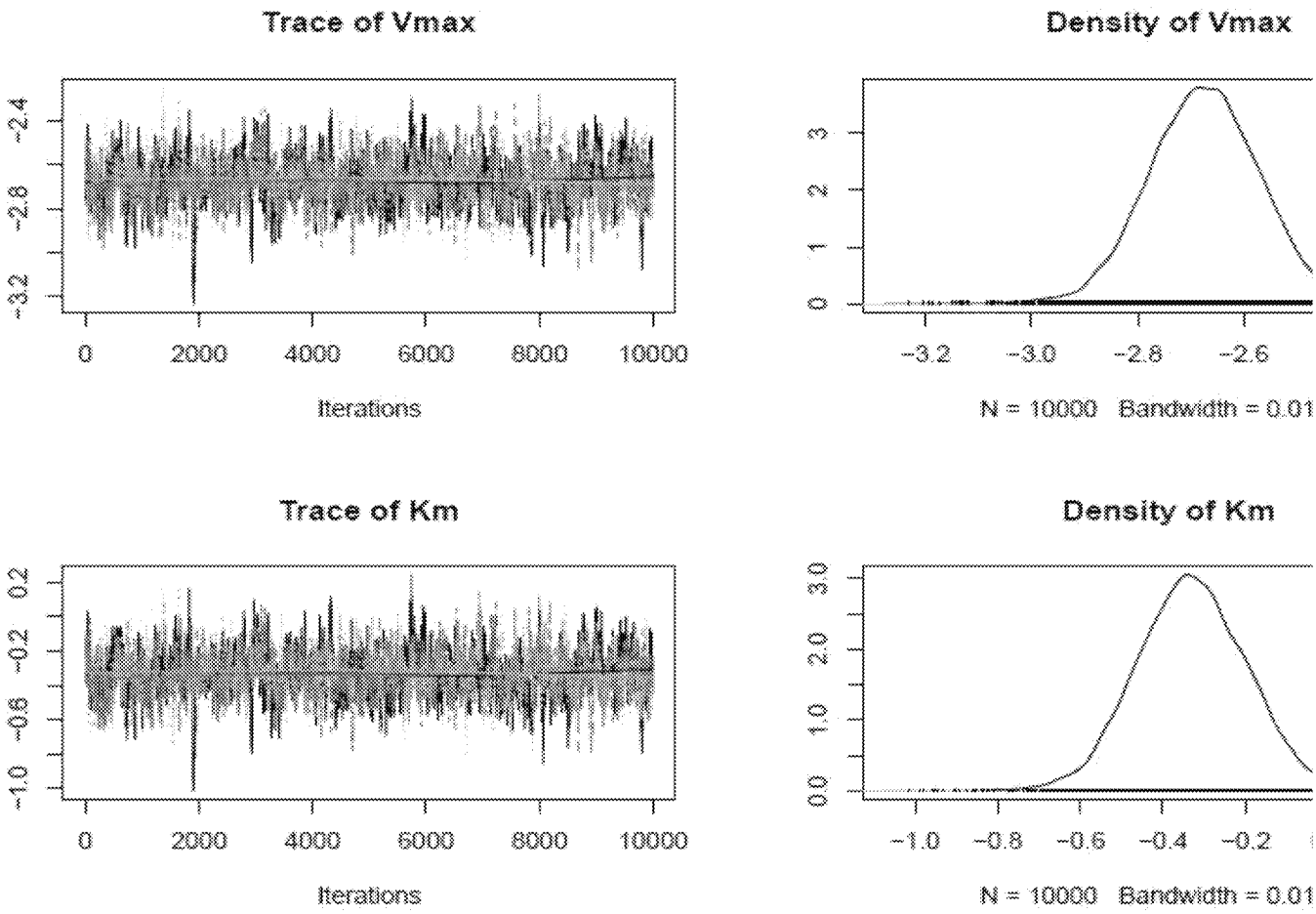
1
= 1
chain = 20000

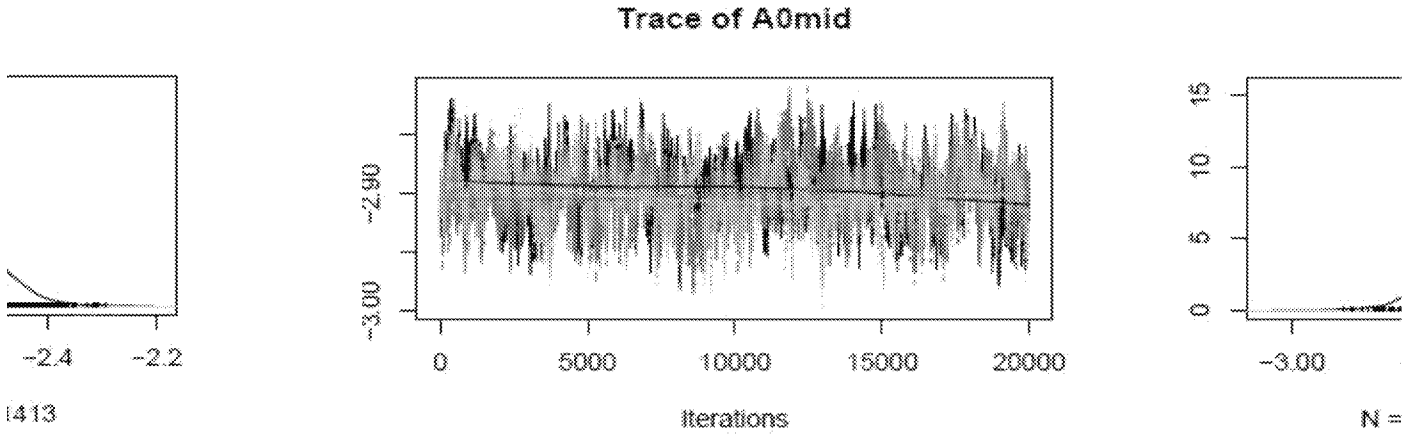
and standard deviation for each variable,
error of the mean:

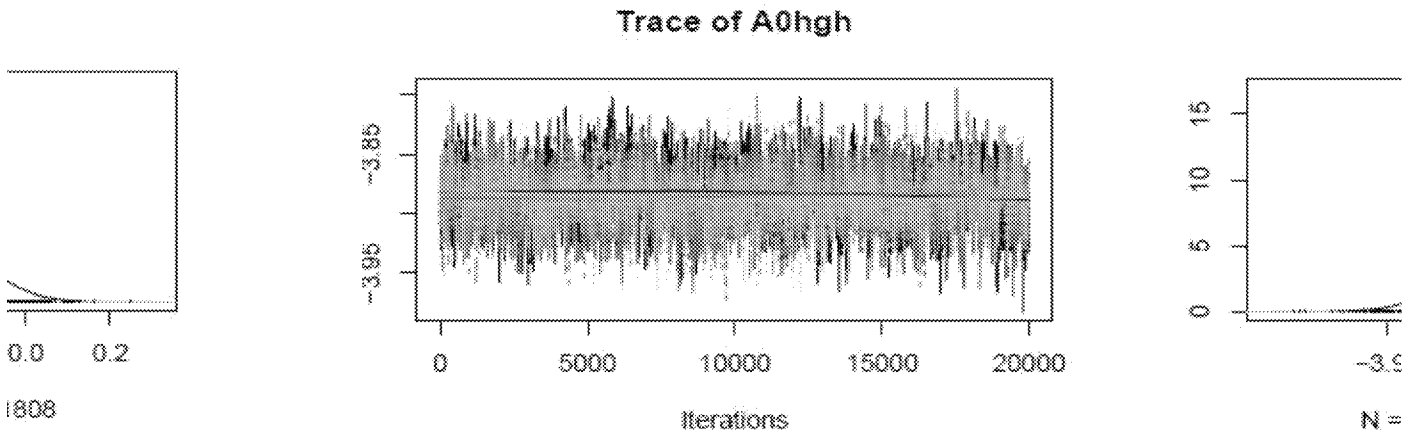
Naive SE	Time-series SE
1.46E-04	0.0013218
1.78E-04	0.0022499
1.63E-04	0.0008569
6.17E-05	0.0001136
3.19E-04	0.0048628
4.75E-04	0.0068441

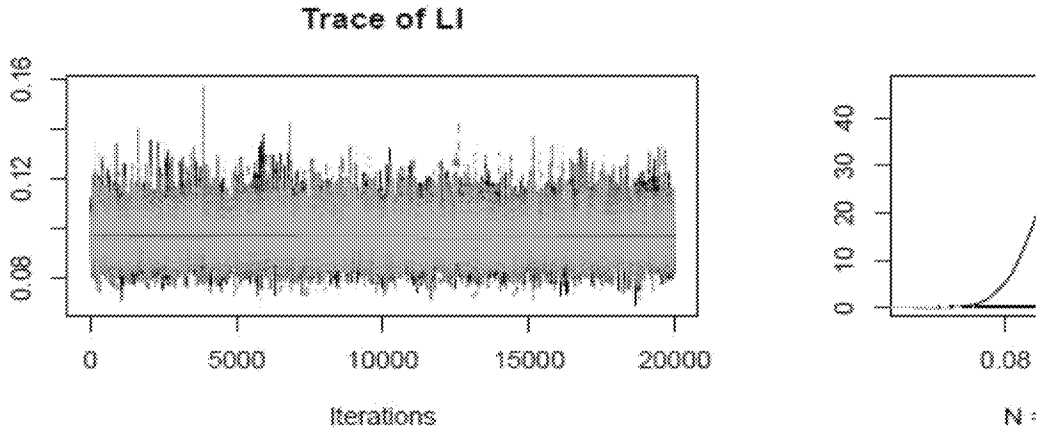
each variable:

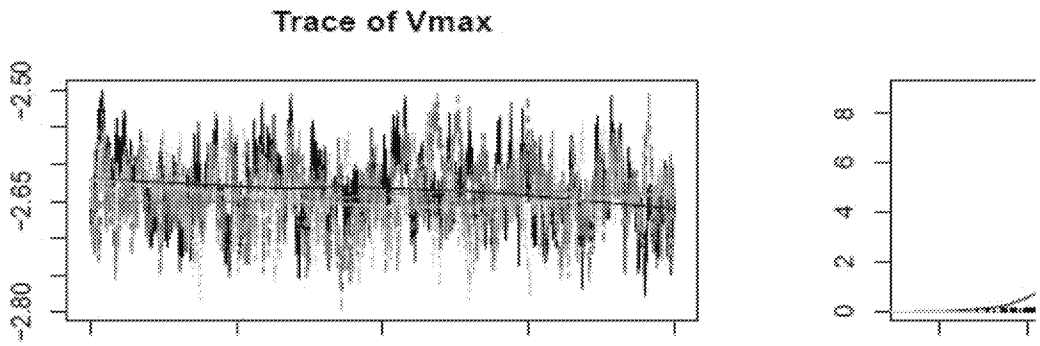
50%	75%	97.50%
-2.18174	-2.1682	-2.1427
-2.90262	-2.8852	-2.856

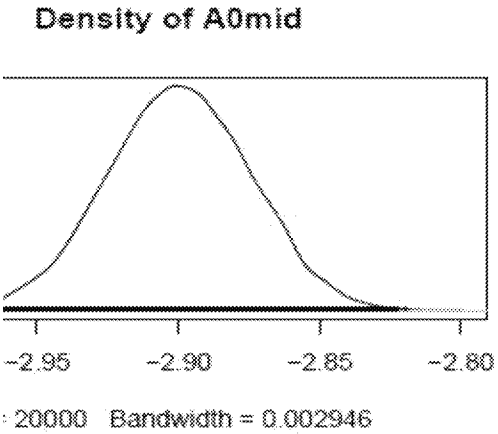

Trace of Vmax
-2.4
-2.8
-3.2
0
2000
4000
6000
8000
10000
Iterations
Density of Vmax
0
1
2
3
-3.2
-3.0
-2.8
-2.6
N = 10000 Bandwidth = 0.01
Trace of Km
0.2
-0.2
-0.6
-1.0
0
2000
4000
6000
8000
10000
Iterations
Density of Km
0.0
1.0
2.0
3.0
-1.0
-0.8
-0.6
-0.4
-0.2
N = 10000 Bandwidth = 0.01

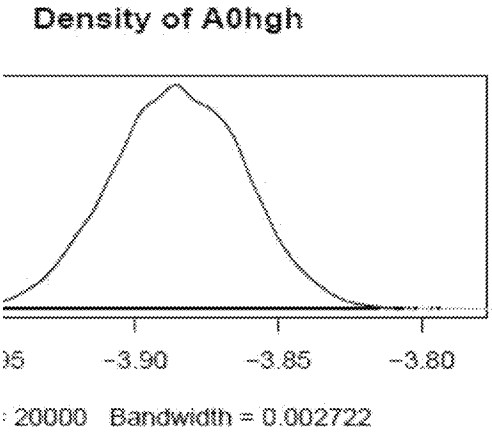

Trace of A0mid
-2.4
-2.2
-2.90
-3.00
0
5000
10000
15000
20000
Iterations
0
5
10
15
-3.00
N =

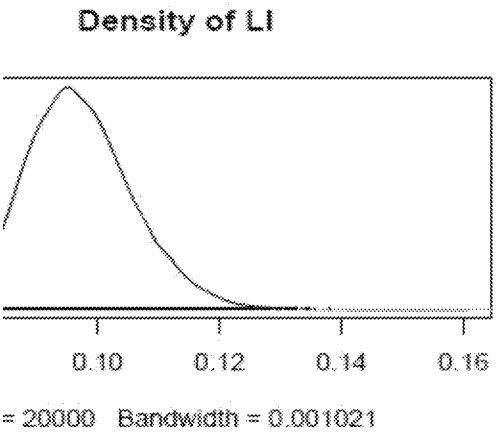

Trace of A0hgh
0.0
0.2
-3.85
-3.95
0
5000
10000
15000
20000
Iterations
0
5
10
15
N =

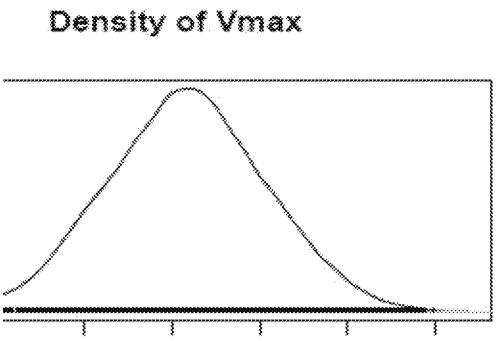

Trace of LI
0.08
0.12
0.16
0
5000
10000
15000
20000
Iterations
0
10
20
30
40
0.08


Trace of Vmax
-2.80
-2.65
-2.50
0
2
4
6
8





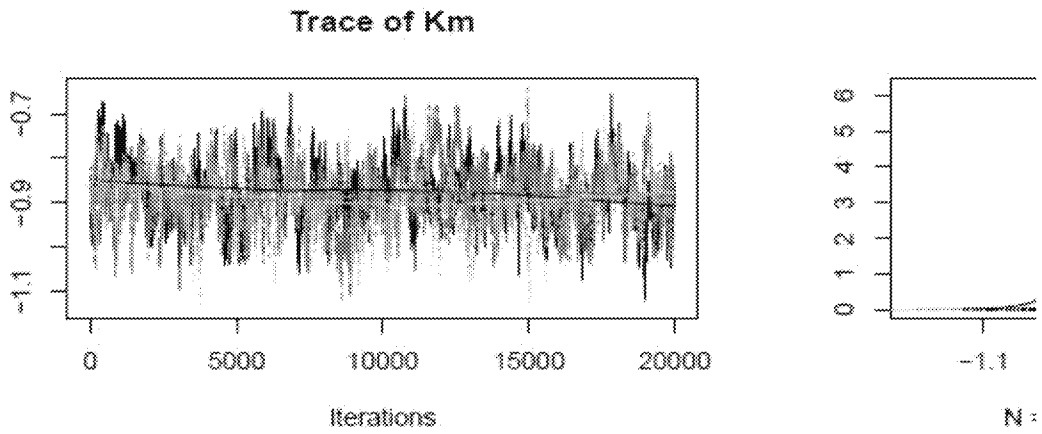




A0hgh	-3.93204	-3.90237
LI	0.08196	0.09088
Vmax	-2.74136	-2.67819
Km	-1.02787	-0.93558

-3.88714	-3.8708	-3.8418
0.09634	0.1024	0.1161
-2.64677	-2.617	-2.563
-0.88916	-0.8467	-0.766

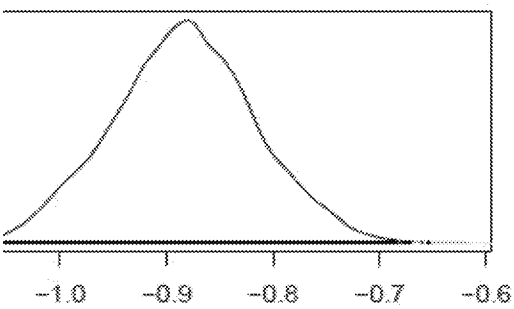
0
5000
10000
15000
20000
−2.80
Iterations
N =


Trace of Km
−0.7
−0.9
−1.1
0
5000
10000
15000
20000
Iterations
0 1 2 3 4 5 6
−1.1
N =

−2.70 −2.60 −2.50

= 20000 Bandwidth = 0.005308

Density of Km



= 20000 Bandwidth = 0.007831

Female

Log **Vmax**
Km

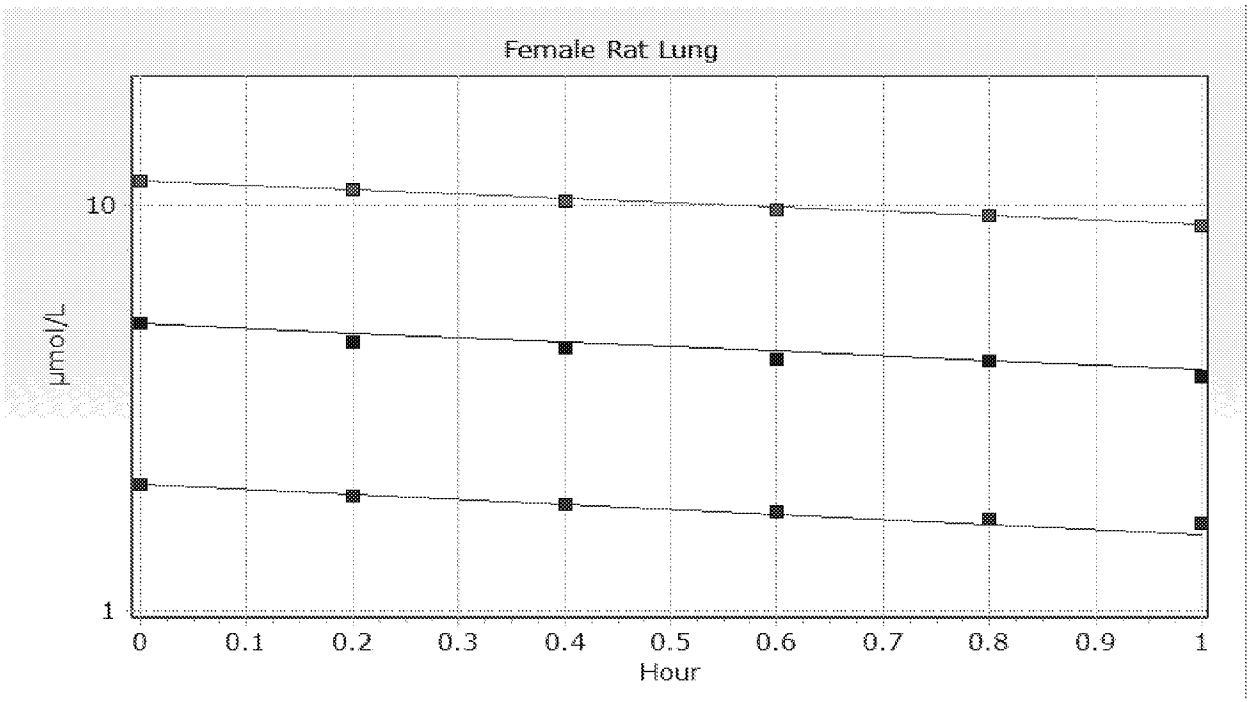
Male

not determinable - data were insufficient to estimate in vitro metabolic parameters.

Female

EXP **Vmax**
Km

Male



	Median
µmol/hr/mg protein	-5.50
µmol/L	Km was set to the posterior median Km estimated for the female mouse lung

	Median

	Median
µmol/hr/mg protein	0.0041
µmol/L	2.369

	Median

95% CI

-6.49 -5.09

95% CI

95% CI

0.0015 0.0062

Female Mouse Lung Km

95% CI

Km was fixed - no parameter correlation plot

```
Female  >           gelman.diag(x,  autoburnin=FALSE)
        Potential   scale           reduction           factors:

                    Point           est.                Upper
        LI                      1                   1
        Vmax                    1                   1

        Multivariate  psrf

                  1
        >
        >           summary(x1)

        Iterations  =               1:10000
        Thinning    interval        =                           1
        Number      of              chains              =
        Sample      size            per                 chain

                  1 Empirical       mean                and
                    plus            standard            error

                    Mean            SD                  Naive
        LI                  0.02868             0.006123    6.12E-05
        Vmax               -5.56714             0.378527    3.79E-03

                  2 Quantiles       for                 each

                            2.50%               25%         50%
        LI                  0.01944             0.02438     0.02768
        Vmax               -6.48618            -5.70219    -5.50231

        >           summary(x2)

        Iterations  =               1:10000
        Thinning    interval        =                           1
        Number      of              chains              =
        Sample      size            per                 chain

                  1 Empirical       mean                and
                    plus            standard            error

                    Mean            SD                  Naive
        LI                  0.02865             0.005728    5.73E-05
        Vmax               -5.55194             0.349512    3.50E-03

                  2 Quantiles       for                 each
```

C.I.

1
= 10000

standard deviation for each variable,
of the mean:

SE Time-series SE
0.0001636
0.0111111

variable:

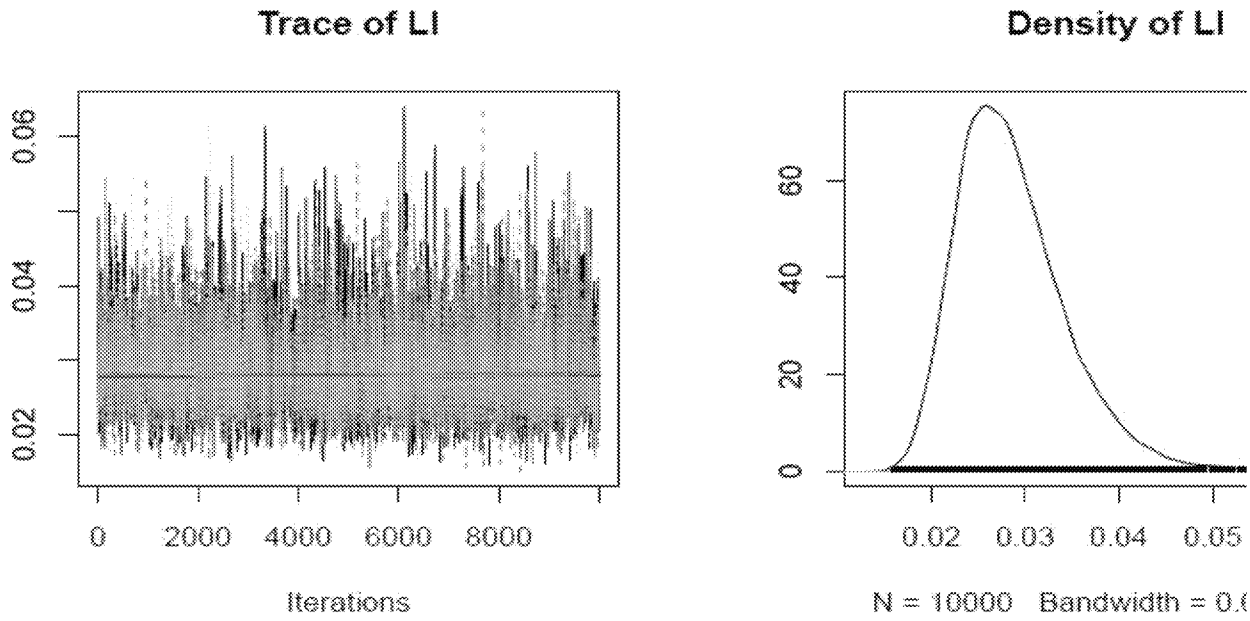
75%	97.50%
0.03187	0.04335
-5.3427	-5.08588

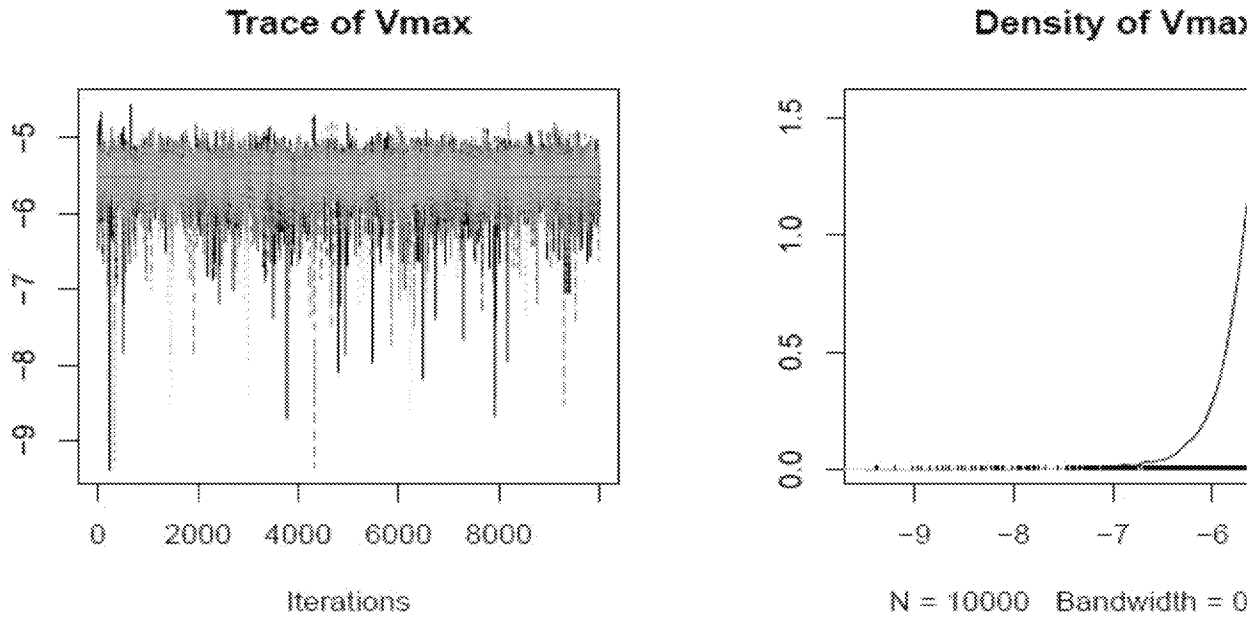
1
= 10000

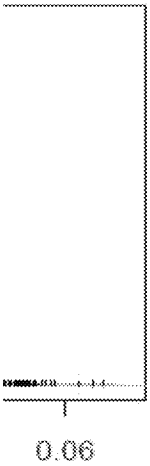
standard deviation for each variable,
of the mean:

SE Time-series SE
0.0001551
0.0098359

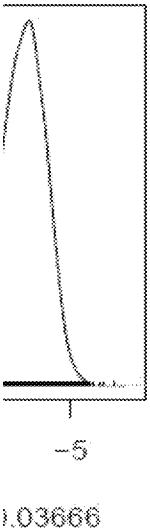
variable:


Trace of LI
0.02
0.04
0.06
0
2000
4000
6000
8000
Iterations
Density of LI
0
20
40
60
0.02
0.03
0.04
0.05
N = 10000 Bandwidth = 0.(


Trace of Vmax
−5
−6
−7
−8
−9
0
2000
4000
6000
8000
Iterations
Density of Vma
0.0
0.5
1.0
1.5
−9
−8
−7
−6
N = 10000 Bandwidth = 0



K



```
                    2.50%          25%      50%
LI                0.01979       0.0245  0.02795
Vmax              -6.3568     -5.6959 -5.49786

>          summary(x3)

Iterations =          1:10000
Thinning   interval   =                       1
Number     of         chains          =
Sample     size       per             chain

         1 Empirical  mean            and
           plus       standard        error

           Mean       SD              Naive
LI              0.02842       0.00567 0.0000567
Vmax             -5.5614       0.36306 0.0036306

         2 Quantiles  for             each

                    2.50%          25%      50%
LI                0.01947       0.02435  0.02765
Vmax             -6.40378     -5.70516 -5.50014

>          summary(x3)

Iterations =          1:19999
Thinning   interval   =                       1
Number     of         chains          =
Sample     size       per             chain

         1 Empirical  mean            and
           plus       standard        error

           Mean       SD              Naive
LI              0.02948       0.03966 0.0002805
Vmax             -5.5651       0.38375 0.0027136

         2 Quantiles  for             each

                    2.50%          25%      50%
LI                0.01964       0.02447  0.02783
Vmax             -6.43208     -5.70606 -5.50156
```

75%	97.50%
0.03191	0.04213
-5.32925	-5.08133

1
= 10000

standard deviation for each variable,
of the mean:

SE Time-series SE
0.000156
0.010678

variable:

75%	97.50%
0.03166	0.0414
-5.34242	-5.0814

1
= 19999

standard deviation for each variable,
of the mean:

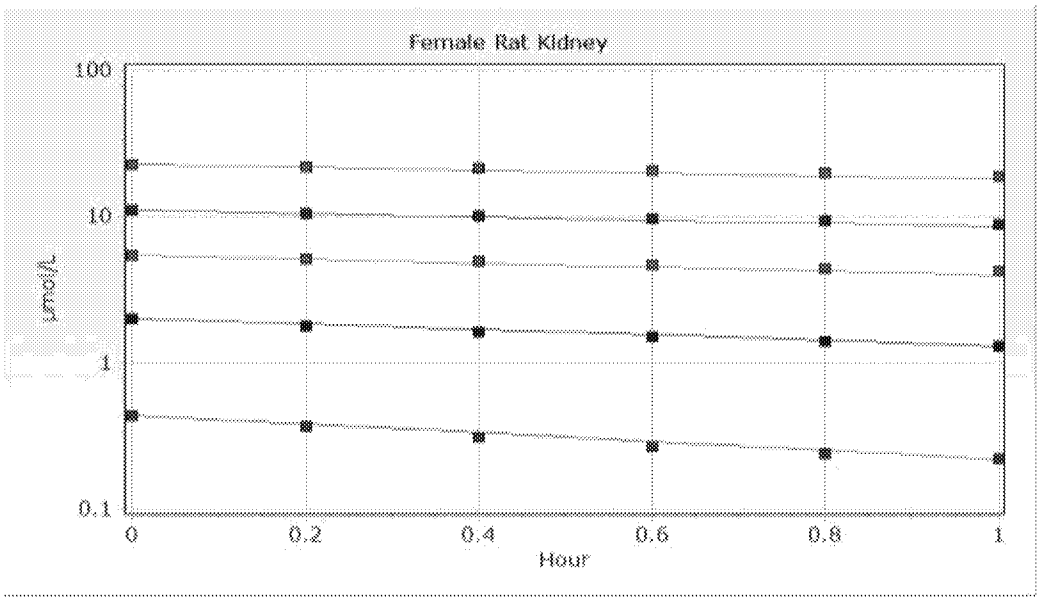
SE Time-series SE
0.0008865
0.008891

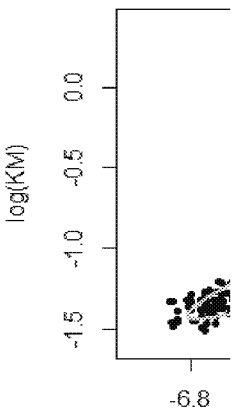
variable:

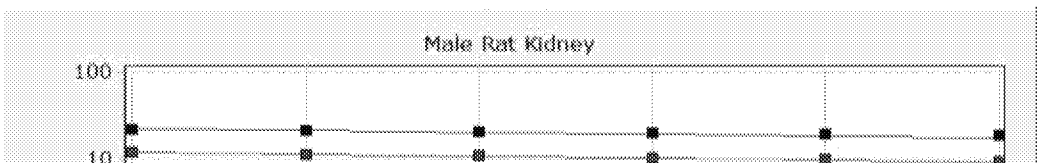
75%	97.50%
0.03183	0.0425
-5.33461	-5.075

			Median	95% CI	
Log	**Female**				
	Vmax	**µmol/hr/mg protein**	-6.296	-6.623	-5.95
	Km	**µmol/L**	-0.801	-1.210	-0.38
	Male				
	Vmax	**µmol/hr/mg protein**	-6.26	-6.55	-5.97
	Km	**µmol/L**	-0.48	-0.83	-0.12

			Median	95% CI	
EXP	**Female**				
	Vmax	**µmol/hr/mg protein**	0.0018	0.0013	0.0026
	Km	**µmol/L**	0.449	0.298	0.687
	Male				
	Vmax	**µmol/hr/mg protein**	0.0019	0.0014	0.0026
	Km	**µmol/L**	0.619	0.437	0.885

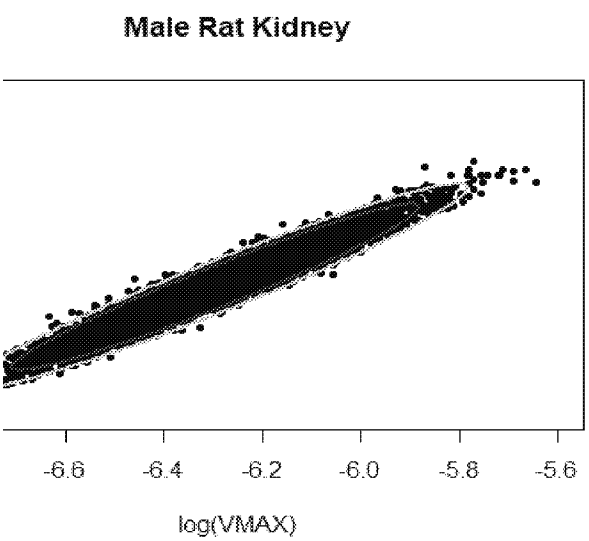


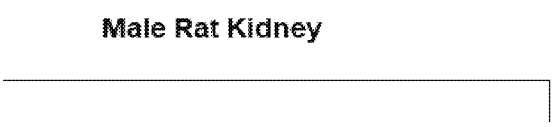




Female

```
> gelman.diag(x, autoburnin=FALSE)
Potential scale reduction

Point est.
LI 1 1
Vmax 1.01 1.04
Km 1.01 1.04

Multivariate psrf

1.01
>
> summary(x1)

Iterations = 1:10000
Thinning interval =
Number of chains
Sample size per

1 Empirical mean
plus standard

Mean SD
LI 0.05662 0.007231
Vmax -6.29482 0.16873
Km -0.79932 0.210893

2 Quantiles for

2.50% 25%
LI 0.04443 0.0517
Vmax -6.62274 -6.4087
Km -1.20987 -0.9407

> summary(x2)

Iterations = 1:10000
Thinning interval =
Number of chains
Sample size per

1 Empirical mean
plus standard

Mean SD
LI 0.05622 0.007031
Vmax -6.28988 0.151785
```





factors:

Upper C.I.

1
= 1
chain = 10000

and standard deviation for each variable,
error of the mean:

Naive SE Time-series SE
7.23E-05 1.51E-04
1.69E-03 1.38E-02
2.11E-03 1.70E-02

each variable:

50% 75% 97.50%
0.05605 0.06083 0.07281
-6.29574 -6.1822 -5.95434
-0.80103 -0.66408 -0.37558

1
= 1
chain = 10000

and standard deviation for each variable,
error of the mean:

Naive SE Time-series SE
7.03E-05 1.30E-04
1.52E-03 1.15E-02

Male > gelman.diag(x,
Potential scale

Point
LI 1
Vmax 1.01
Km 1.01

Multivariate psrf

1.01
>
> summary(x1)

Iterations =
Thinning interval
Number of
Sample size

1 Empirical
plus

Mean
LI 0.04133
Vmax -6.26242
Km -0.47954

2 Quantiles

2.50%
LI 0.03258
Vmax -6.54539
Km -0.82721

> summary(x2)

Iterations =
Thinning interval
Number of
Sample size

1 Empirical
plus

Mean
LI 0.04152
Vmax -6.23691

autoburnin=FALSE)
reduction factors:

est.	Upper C.I.
1	
1.02	
1.02	

1:10000
= 1
chains = 1
per chain = 10000

mean and standard deviation for each variable,
standard error of the mean:

SD	Naive SE	Time-series SE
0.005319	5.32E-05	1.06E-04
0.14787	1.48E-03	1.25E-02
0.180938	1.81E-03	1.51E-02

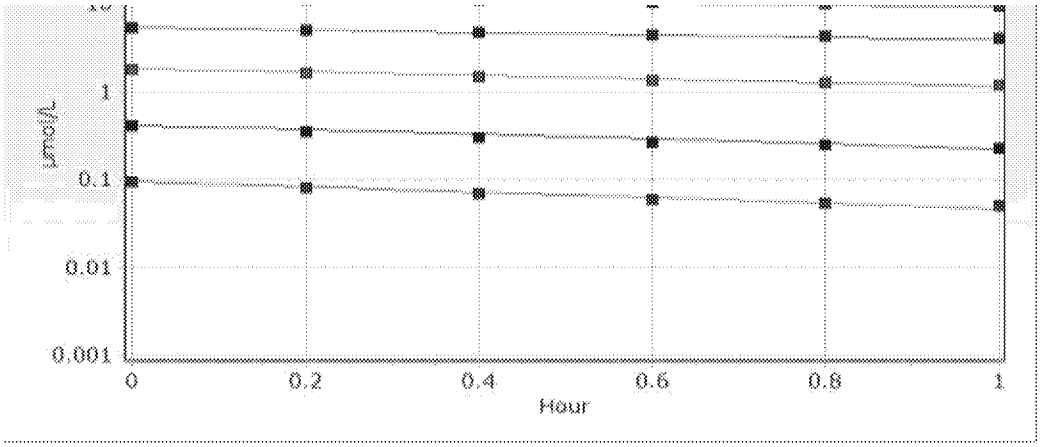
for each variable:

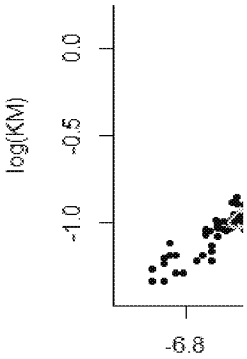
25%	50%	75%	97.50%
0.03763	0.04073	0.04461	0.05337
-6.36184	-6.26163	-6.15961	-5.9715
-0.60111	-0.47992	-0.3559	-0.12203

1:10000
= 1
chains = 1
per chain = 10000

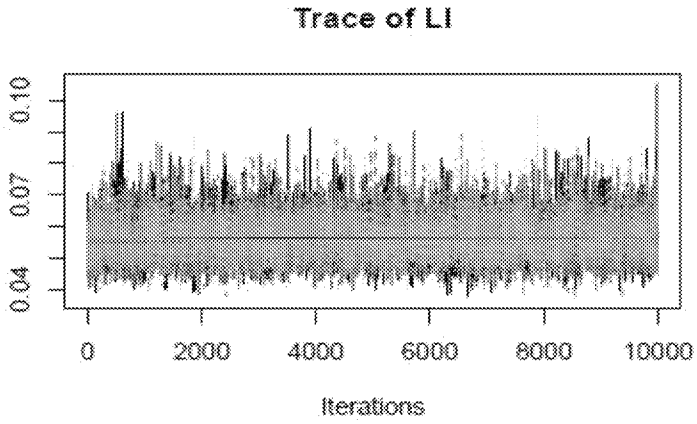
mean and standard deviation for each variable,
standard error of the mean:

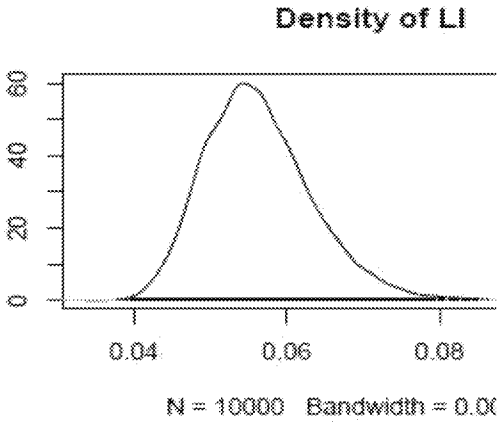
SD	Naive SE	Time-series SE
0.005321	5.32E-05	1.19E-04
0.157309	1.57E-03	1.43E-02

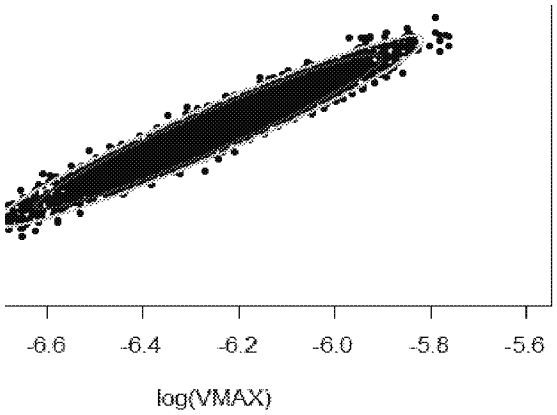

μmol/L
1
0.1
0.01
0.001
0
0.2
0.4
0.6
0.8
1
Hour


log(KM)
0.0
-0.5
-1.0
-6.8

Female Rat


Trace of LI
0.10
0.07
0.04
0
2000
4000
6000
8000
10000
Iterations


Density of LI
60
40
20
0
0.04
0.06
0.08
N = 10000 Bandwidth = 0.0(



Km	-0.79265	0.187731

2 Quantiles for

	2.50%	25%
LI	0.04458	0.05109
Vmax	-6.56963	-6.39944
Km	-1.1409	-0.92657

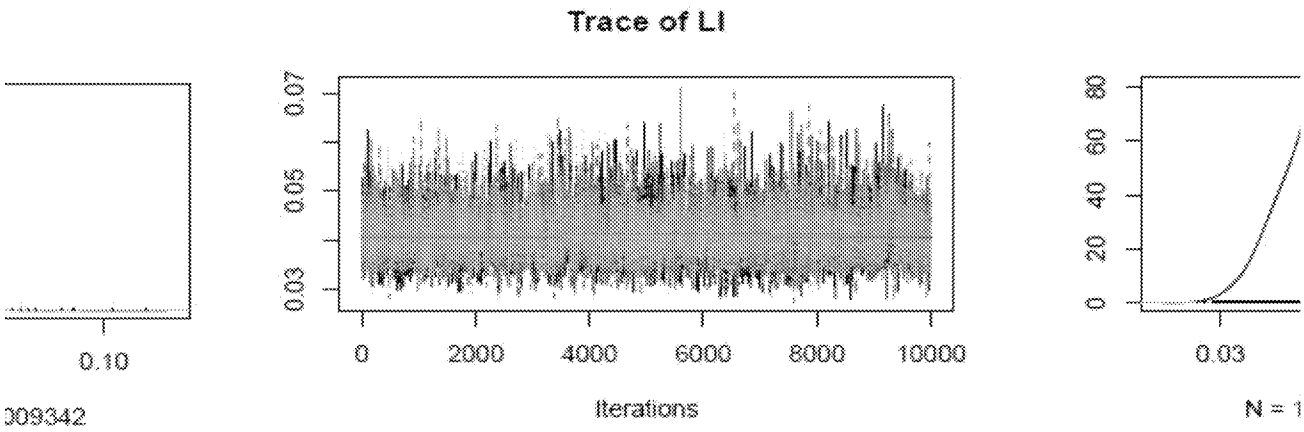
```
> summary(x3)

Iterations = 1:10000
Thinning interval =
Number of chains
Sample size per

1 Empirical mean
plus standard
```

	Mean	SD
LI	0.05624	0.007086
Vmax	-6.32732	0.168075
Km	-0.84048	0.208097

2 Quantiles for

	2.50%	25%
LI	0.04445	0.05121
Vmax	-6.65409	-6.44297
Km	-1.24452	-0.98248

Male Rat



Trace of Vmax

1.88E-03 1.39E-02

each variable:

50%	75%	97.50%
0.05554	0.0605	0.07182
-6.29166	-6.1871	-5.98069
-0.79655	-0.6641	-0.41202

1
= 1
chain = 10000

and standard deviation for each variable,
error of the mean:

Naive SE	Time-series SE
7.09E-05	1.23E-04
1.68E-03	1.36E-02
2.08E-03	1.71E-02

each variable:

50%	75%	97.50%
0.05545	0.0604	0.07244
-6.3222	-6.211	-6.00152
-0.83255	-0.6972	-0.44368

Km -0.44958

2 Quantiles

	2.50%
LI	0.03273
Vmax	-6.56376
Km	-0.85279

> summary(x3)

Iterations =
Thinning interval
Number of
Sample size

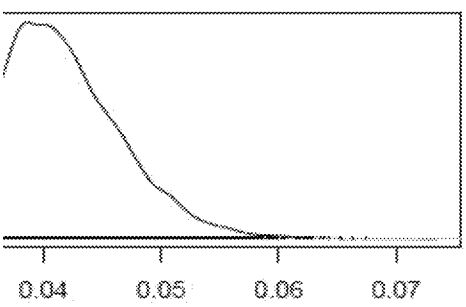
1 Empirical
plus

	Mean
LI	0.04136
Vmax	-6.23539
Km	-0.44846

2 Quantiles

	2.50%
LI	0.03274
Vmax	-6.56829
Km	-0.84996

Density of LI



10000 Bandwidth = 0.0006917

0.19248	1.93E-03	1.73E-02

for each variable:

25%	50%	75%	97.50%
0.03785	0.04093	0.04464	0.05351
-6.33595	-6.22942	-6.13253	-5.95229
-0.57125	-0.44044	-0.32239	-0.09631

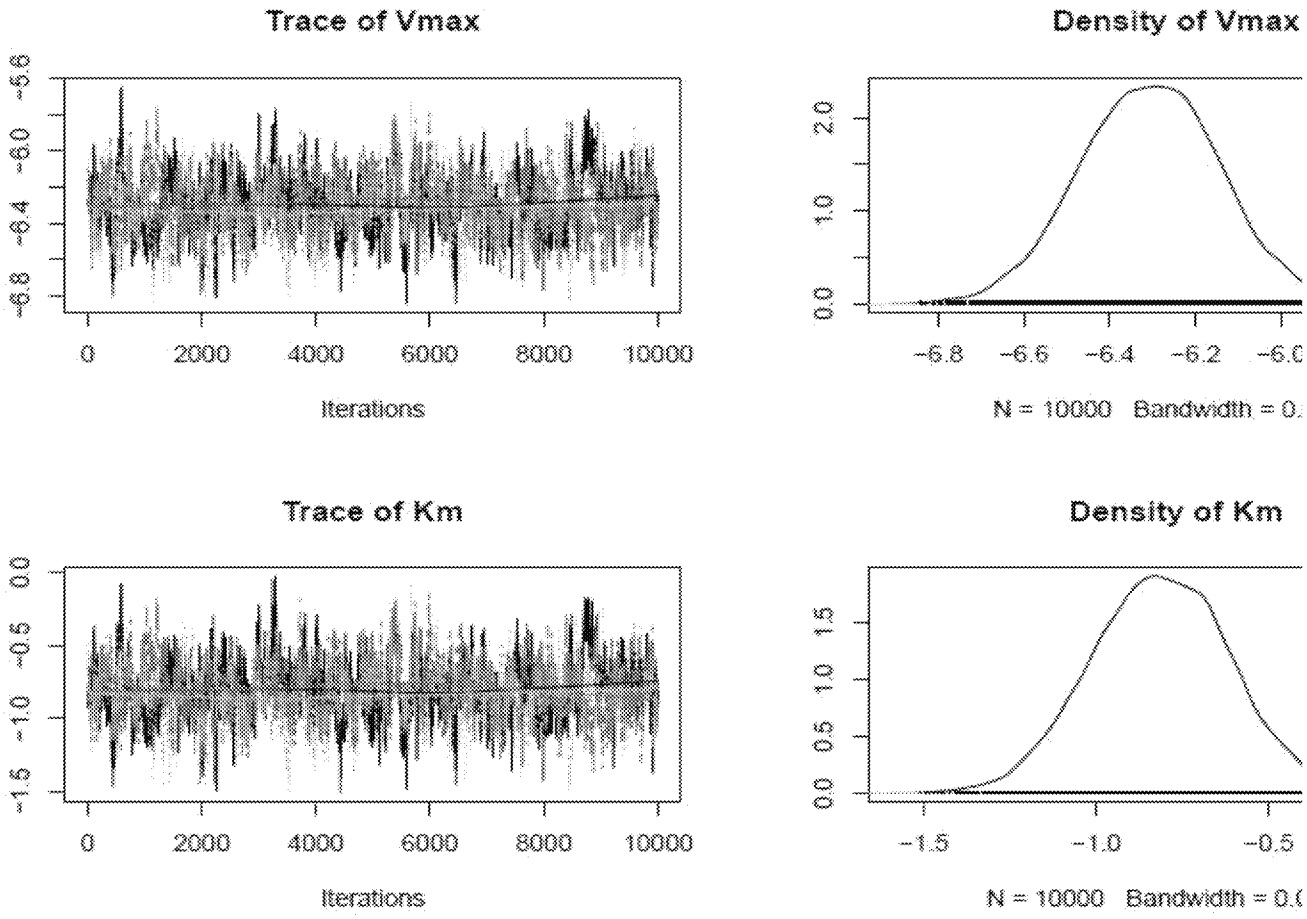
1:10000
= 1
chains = 1
per chain = 10000

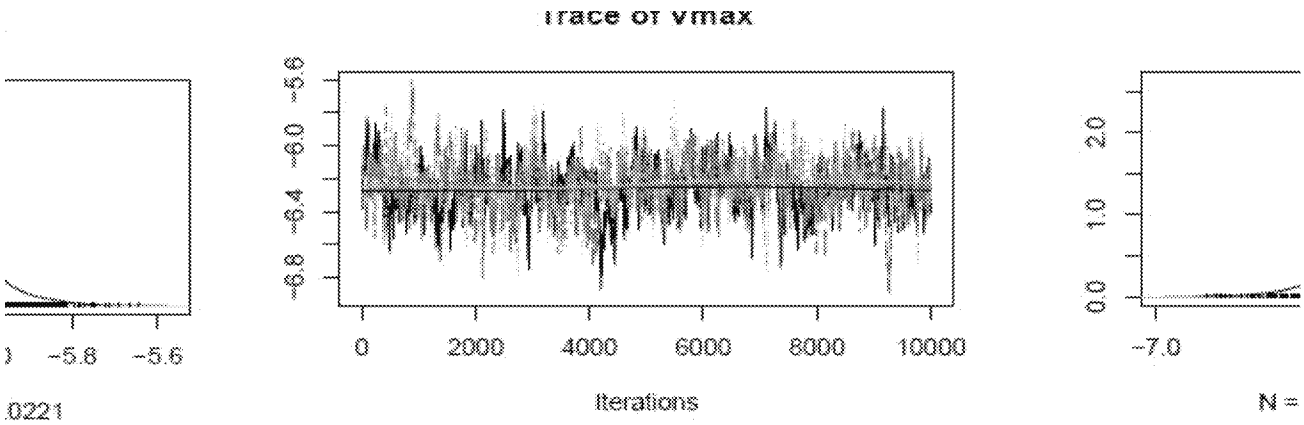
mean and standard deviation for each variable,
standard error of the mean:

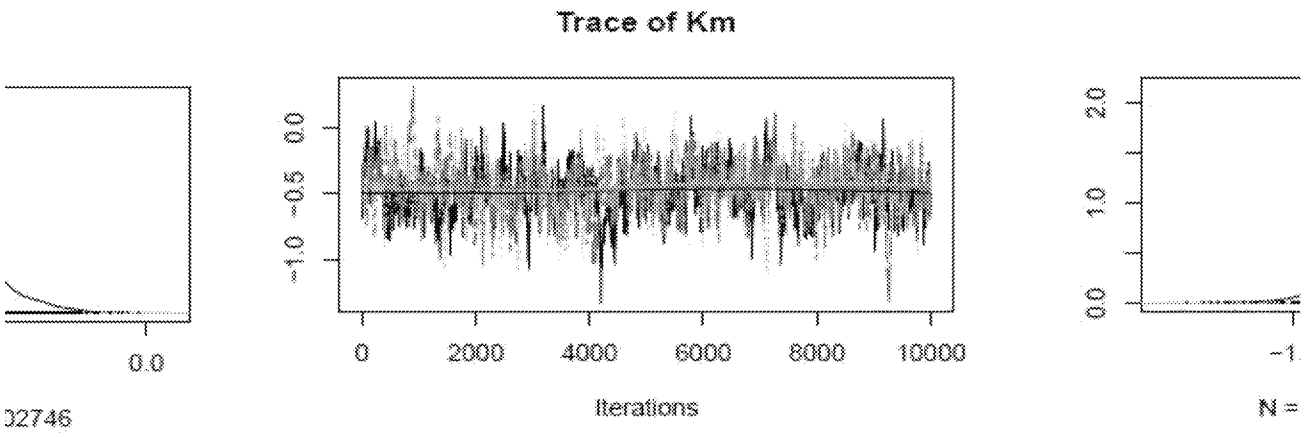
SD	Naive SE	Time-series SE
0.005238	5.24E-05	9.87E-05
0.157025	1.57E-03	1.42E-02
0.190374	1.90E-03	1.74E-02

for each variable:

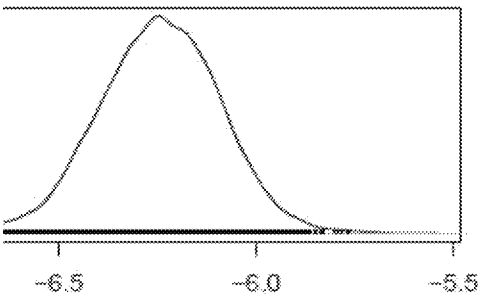
25%	50%	75%	97.50%
0.03764	0.04079	0.04445	0.05295
-6.3321	-6.2347	-6.12857	-5.9325
-0.56595	-0.44479	-0.31943	-0.07425


Trace of Vmax
-6.8
-6.4
-6.0
-5.6
0
2000
4000
6000
8000
10000
Iterations
Density of Vmax
0.0
1.0
2.0
-6.8
-6.6
-6.4
-6.2
N = 10000 Bandwidth = 0.
Trace of Km
-1.5
-1.0
-0.5
0.0
0
2000
4000
6000
8000
10000
Iterations
Density of Km
0.0
0.5
1.0
1.5
-1.5
-1.0
-0.5
N = 10000 Bandwidth = 0.


Trace of Vmax
−5.6
−6.0
−6.4
−6.8
0
2000
4000
6000
8000
10000
Iterations
2.0
1.0
0.0
−7.0
−5.8
−5.6
.0221
N =

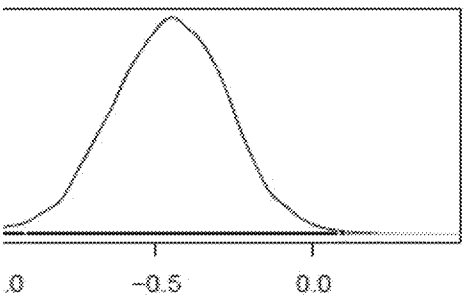

Trace of Km
0.0
−0.5
−1.0
0
2000
4000
6000
8000
10000
Iterations
2.0
1.0
0.0
0.0
−1.
02746
N =

Density of Vmax



10000 Bandwidth = 0.02062

Density of Km



10000 Bandwidth = 0.02522

Mixed Human with estimation of the start vial amount as part of the MCMC

Log

A0low
A0mid
A0hgh

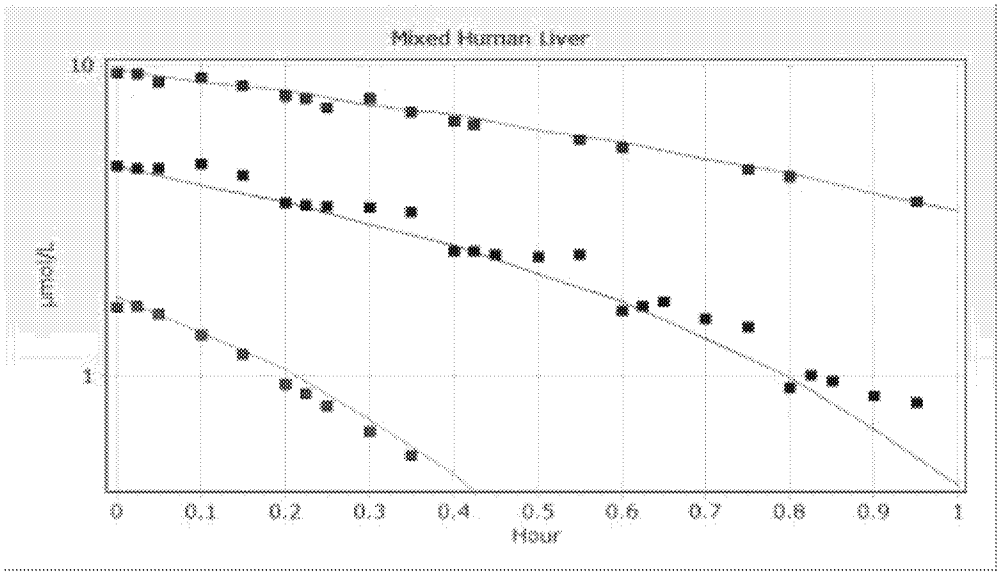
Vmax
Km

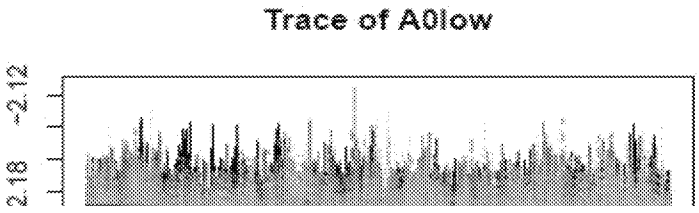
Mixed Human

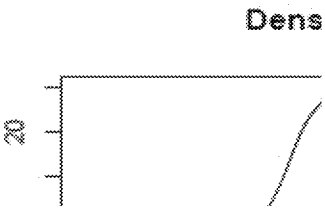
EXP

A0low
A0mid
A0hgh

Vmax
Km

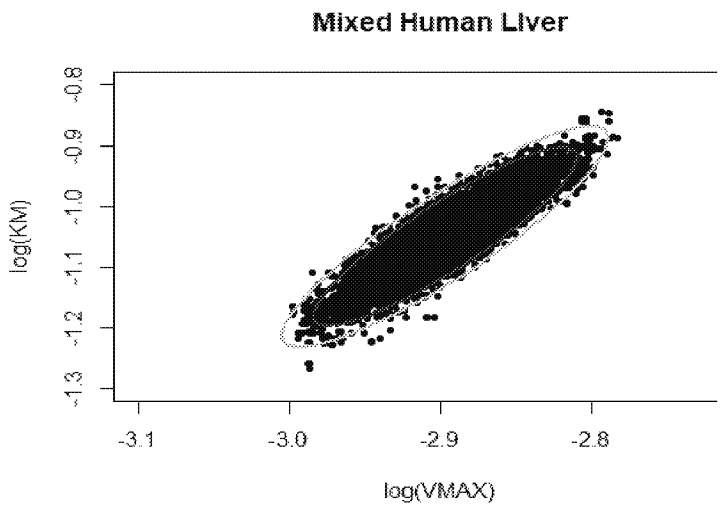




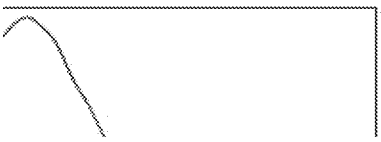


	Median	95% CI	
µmol	-2.19256	-2.22353	-2.16093
µmol	-2.83933	-2.87308	-2.80278
µmol	-3.92429	-3.96151	-3.88714
µmol/hr/mg protein	-2.89851	-2.96397	-2.82594
µmol/L	-1.05319	-1.1657	-0.93204

	Median	95% CI	
µmol	0.112	0.108	0.115
µmol	0.058	0.057	0.061
µmol	0.020	0.019	0.021
µmol/hr/mg protein	0.055	0.052	0.059
µmol/L	0.349	0.312	0.394



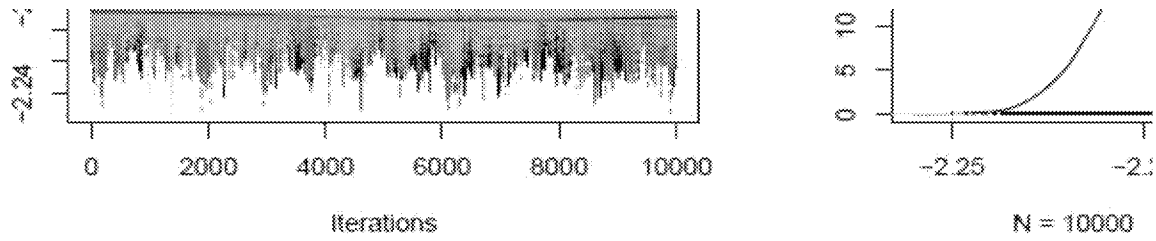
ity of A0low



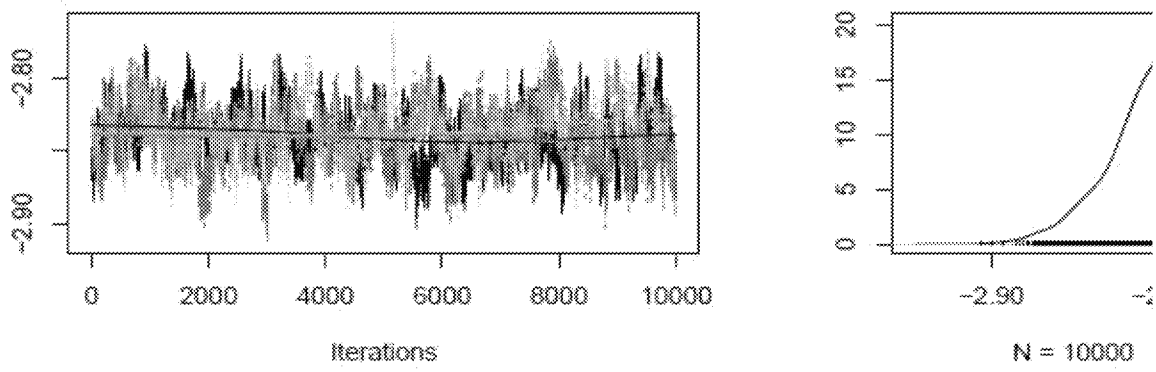
```
>          gelman.diag(x,   autoburnin=FALSE)
Potential  scale            reduction          factors:

           Point            est.               Upper    C.I.
A0low                 1.01                1.02
A0mid                 1.02                1.05
A0hgh                    1                1.01
LI                       1                   1
Vmax                  1.02                1.06
Km                    1.02                1.06

Multivariate  psrf

        1.01
>
>          summary(x1)

Iterations =            1:10000
Thinning   interval     =                   1
Number     of           chains              =          1
Sample     size         per                 chain      =          10000

         1 Empirical    mean                and        standard   deviation  for    each
           plus         standard            error      of         the        mean:

           Mean         SD                  Naive      SE         Time-series SE
A0low            -2.19232          0.015852  1.59E-04  0.0008077
A0mid             -2.8389          0.018107  1.81E-04  0.0017595
A0hgh            -3.92455          0.018913  1.89E-04   0.000857
LI                0.07132          0.006924  6.92E-05  0.0001281
Vmax             -2.89635          0.035633  3.56E-04  0.0040625          1.2%
Km               -1.04993          0.059886  5.99E-04  0.0058665         -5.7%

         2 Quantiles    for                 each       variable:

                2.50%            25%        50%        75%        97.50%
A0low           -2.22353         -2.20299   -2.19256   -2.18188   -2.16093
A0mid           -2.87308         -2.85165   -2.83933   -2.82698   -2.80278
A0hgh           -3.96151         -3.93707   -3.92429   -3.9118    -3.88714
LI               0.05933          0.06657    0.07076    0.07569    0.08651
Vmax            -2.96397         -2.92079   -2.89851   -2.87194   -2.82594
Km               -1.1657          -1.0915   -1.05319   -1.00669   -0.93204

>          summary(x2)

Iterations =            1:10000
Thinning   interval     =                   1
```

-2.7

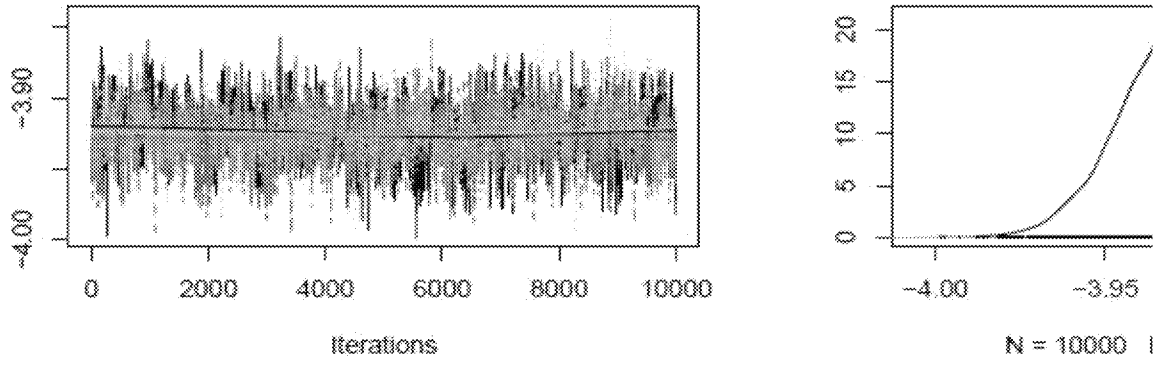
variable,



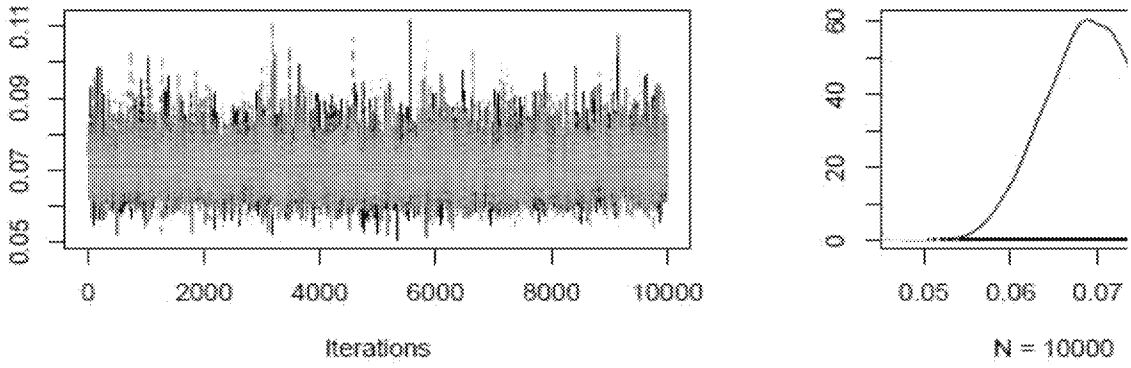
Trace of A0mid **Dens**



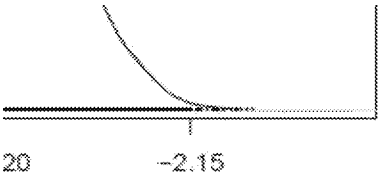
Trace of A0hgh **Dens**



Trace of LI **De**

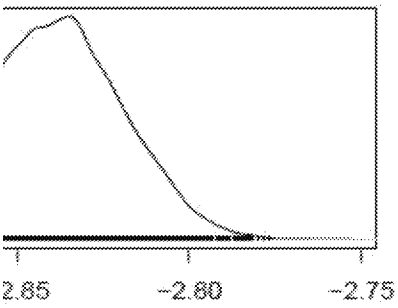


Trace of Vmax **Den**



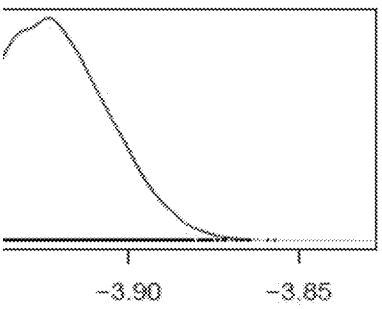
Bandwidth = 0.00216

ity of A0mid



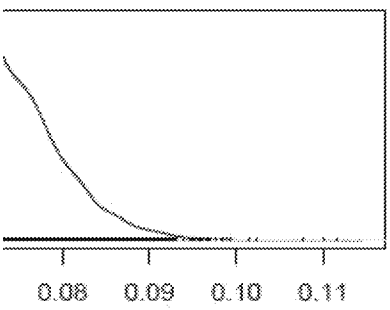
Bandwidth = 0.00262

ity of A0hgh



Bandwidth = 0.002513

ensity of LI



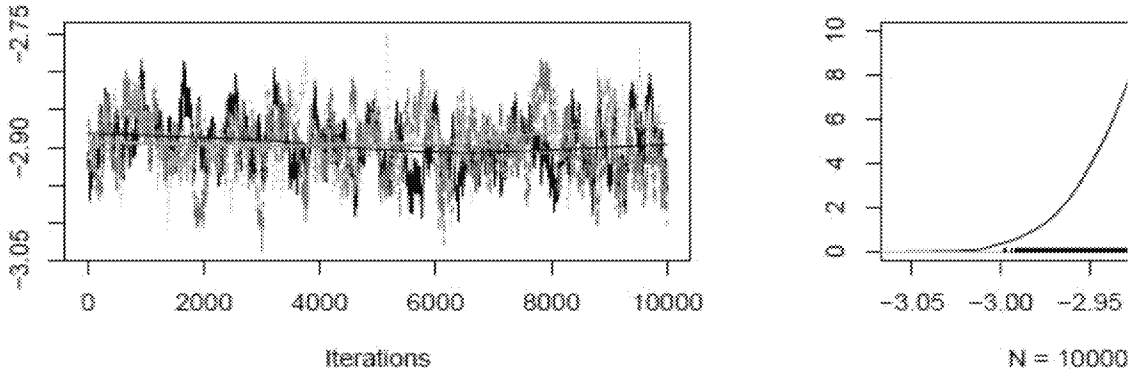
Bandwidth = 0.000922

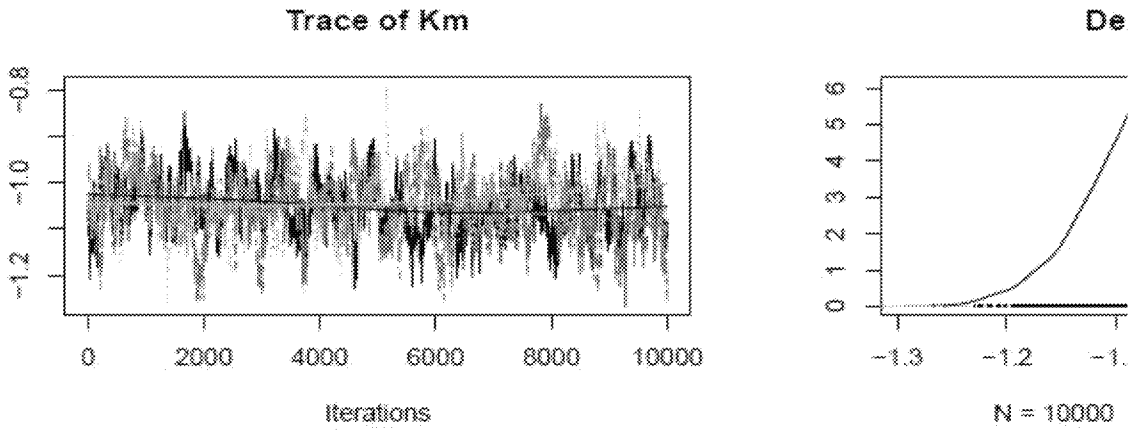
sity of Vmax

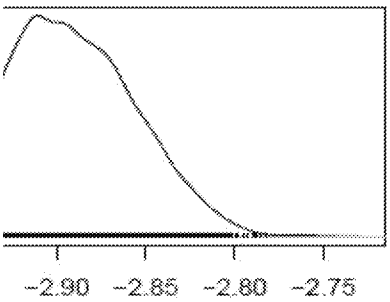
```
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each
  plus standard error of the mean:

  Mean SD Naive SE Time-series SE
A0low -2.19328 0.016581 1.66E-04 0.0011853
A0mid -2.84086 0.020773 2.08E-04 0.002357
A0hgh -3.92683 0.018807 1.88E-04 0.0008175
LI 0.07138 0.006975 6.98E-05 0.0001363
Vmax -2.90091 0.04251 4.25E-04 0.005455
Km -1.05555 0.071698 7.17E-04 0.0087422

2 Quantiles for each variable:

  2.50% 25% 50% 75% 97.50%
A0low -2.22631 -2.20397 -2.19344 -2.1823 -2.16052
A0mid -2.88147 -2.85532 -2.84064 -2.8269 -2.79926
A0hgh -3.96375 -3.93971 -3.92675 -3.9137 -3.89062
LI 0.05924 0.06657 0.07072 0.0757 0.08682
Vmax -2.98513 -2.92965 -2.90049 -2.8719 -2.81852
Km -1.20086 -1.10378 -1.05501 -1.0072 -0.91386

> summary(x3)

Iterations = 1:10000
Thinning interval = 1
Number of chains = 1
Sample size per chain = 10000

1 Empirical mean and standard deviation for each
  plus standard error of the mean:

  Mean SD Naive SE Time-series SE
A0low -2.19044 0.016032 1.60E-04 0.0008406
A0mid -2.83577 0.018977 1.90E-04 0.0019416
A0hgh -3.92451 0.018085 1.81E-04 0.0007944
LI 0.07119 0.006943 6.94E-05 0.0001283
Vmax -2.88915 0.038568 3.86E-04 0.00492
Km -1.03687 0.06539 6.54E-04 0.00743

2 Quantiles for each variable:

  2.50% 25% 50% 75% 97.50%
A0low -2.2218 -2.20109 -2.19063 -2.17991 -2.15882
A0mid -2.87203 -2.84939 -2.83582 -2.82276 -2.79822
```

variable,

variable,

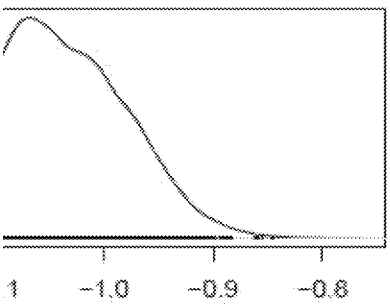

-2.75
-2.90
-3.05
0
2000
4000
6000
8000
10000
Iterations
0
2
4
6
8
10
-3.05
-3.00
-2.95
N = 10000


Trace of Km
De
-0.8
-1.0
-1.2
0
2000
4000
6000
8000
10000
Iterations
0
1
2
3
4
5
6
-1.3
-1.2
-1.
N = 10000



Bandwidth = 0.0053

nsity of Km



Bandwidth = 0.008941

A0hgh	-3.95991	-3.93657	-3.92467	-3.91274	-3.88842
LI	0.05907	0.06629	0.07069	0.07557	0.08615
Vmax	-2.95902	-2.91722	-2.89031	-2.86281	-2.81374
Km	-1.1583	-1.08281	-1.04049	-0.99046	-0.90831

Mixed Human Lung Microsomes

not determinable - data were insufficient to estimate in vitro metabolic parameters.

Mean	95% CI

MCMC Mean Parameters

			Liver			Lung		
			Mean	95% CI		Mean	95% CI	
Kg estimated	**Male Mouse**	**Vmax (µmol/hr/mg protein)**	0.212	0.161	0.257	0.085	0.069	0.105
		Km (µmol/L)	0.689	0.472	0.903	1.194	0.943	1.523
	Female Mouse	**Vmax (µmol/hr/mg protein)**	0.105	0.087	0.127	0.022	0.015	0.031
		Km (µmol/L)	0.448	0.302	0.652	2.369	1.555	3.549
	Male Rat	**Vmax (µmol/hr/mg protein)**	0.072	0.066	0.078	ND*		
		Km (µmol/L)	0.417	0.367	0.477			
	Female Rat	**Vmax (µmol/hr/mg protein)**	0.069	0.056	0.085	0.00408	0.00152	0.00618
		Km (µmol/L)	0.718	0.544	0.933	2.369		
	Human	**Vmax (µmol/hr/mg protein)**	0.055	0.052	0.059	7.88E-05	**Alternative approach**	
		Km (µmol/L)	0.349	0.312	0.394	3.49E-01		

* ND: not determinable

Female Rat Lung Km was fixed to Female Mouse Km for the MCMC

Kidney		
Mean	**95% CI**	
0.012	0.0088	0.015
0.647	0.469	0.902
ND*		
0.0019	0.0014	0.0026
0.619	0.437	0.885
0.0018	0.0013	0.0026
0.449	0.298	0.687

Not Measured

Species
Male Mouse
Female Mouse
Male Rat
Female Rat
Human

Scaling factors for average adults in each species

Summary In Vivo Parameters
Parameter
Vmax (mg/hr/BW^0.75)
Km (mg/L)
Vmax (mg/hr/BW^0.75)
Km (mg/L)
Vmax (mg/hr/BW^0.75)
Km (mg/L)
Vmax (mg/hr/BW^0.75)
Km (mg/L)
Vmax (mg/hr/BW^0.75)
Km (mg/L)

Revised Scaling

Parameter
B6C3F1 Mouse (Female)
B6C3F1 Mouse (Male)
F344 Rat (Female)
F344 Rat (Male)
Average Human

Liver	Lung	Kidney
16.09	0.49	0.14
0.061	0.11	0.057
7.99	0.12	ND*
0.040	0.21	
7.42	ND*	0.018
0.037		0.055
6.36	0.03	0.015
0.064	0.21	0.040
14.51	0.0031	
0.031	0.031	

* ND: not determinable

BW (kg)	Liver fractional weight (VLC)	Lung fractional weight (VLUC)	Kidney fractional weight (VKC)	Liver mg microsomal protein per g liver (MPPGL)
0.04	0.0549	0.0073	0.0167	35
0.04	0.0549	0.0073	0.0167	35
0.256	0.0366	0.005	0.0073	40
0.407	0.0366	0.005	0.0073	40
70	0.0257	0.0076	0.0044	40

Lung mg microsomsal protein per g lung (MPPGLU)	Kidney mg microsomal protein per g kidney (MPPGK)	MW
20	18	88.53650
20	18	g/mol = ug/umol
20	18	
20	18	
20	11	

Biological Scaling	Vmaxc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight	/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
Female Mouse	Values	0.105	35	8.07	90.19	7.99
LIVER	Scaling & calculation		x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
	Unit	umol/h/mg MP	umol/h/g liver	umol/h	umol/h/kg BW^0.75	mg/h/kg BW^0.75

Biological Scaling	Vmaxc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight	/BW^0.75	x MW = In vivo parameter (unit in PBPK model)

Biological Scaling	VmaxLUc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight
Female Mouse	Values	0.022	20	**0.126**
LUNG	Scaling & calculation		x MPPGLU (mg MP/g lung)	x BW (kg) X VLUC X 1000 (g/kg)
	Unit	umol/h/mg MP	umol/h/g lung	umol/h

Biological Scaling	VmaxLUc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight

/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
1.41	0.12
/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
umol/h/kg BW^0.75	mg/h/kg BW^0.75

/BW^0.75	x MW = In vivo parameter (unit in PBPK model)

Biological Scaling	VmaxKIDc (mg/h/kg BW^0.75)	In vitro value (Yang et al. 2012, Table 3)	x Scaling factor	x Tissue weight

/BW^0.75	x MW = In vivo parameter (unit in PBPK model)

References

Reference

1. Brown et al., 1997, Toxicol. Ind. Health, July-Aug;13(4):407-84. Review. PubMed PMID:9249
2. Barter et al., Drug Metab Dispos. 2008 Dec;36(12):2405-9. doi: 10.1124/dmd.108.021311. E
3. Himmelstein et al., Toxicol Sci. 2004b May;79(1):28-37. Epub 2004 Feb 19. PubMed PMID: 1
4. Houston and Galetin, Curr Drug Metab. 2008 Nov;9(9):940-51. Review. PubMed PMID: 189
5. Scotcher et al., Drug Metab Dispos. 2017 May;45(5):556-568. doi: 10.1124/dmd.117.07524

Brown et al, 1997 (page 415 in text)	Brown et al, 1997 (Tables 4, 5, & 7)	Brown et al, 1997 (Tables 4, 5, & 7)	Brown et al, 1997 (Tables 4, 5, & 7)	Medinsky et al., 1994 for mouse; Medinsky et al., 1994 and Houston and Galetin, 2008 for rat; Barter et al., 2008 2007 for human

)929
:pub 2008 Sep 5. PubMed PMID: 18775982.

14976335.

91591.

2. Epub 2017 Mar 7. PubMed PMID: 28270564; PubMed Central PMCID: PMC5399648.

Medinsky et al., 1994 for all species	Yoon et al., 2007 for mouse and rat; Scotcher et al., 2017 for human	

Male Mouse	Values	0.212	35	16.26	181.77	16.09
LIVER	Scaling & calculation		x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
	Unit	umol/h/mg MP	umol/h/g liver	umol/h	umol/h/kg BW^0.75	mg/h/kg BW^0.75

Biological Scaling	Vmaxc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight	/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
Female Rat	Values	0.069	40	25.87	71.89	6.36
LIVER	Scaling & calculation		x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
	Unit	umol/h/mg MP	umol/h/g liver	umol/h	umol/h/kg BW^0.75	mg/h/kg BW^0.75

Biological Scaling	Vmaxc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight	/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
Male Rat	Values	0.072	40	42.70	83.80	7.42
LIVER	Scaling & calculation		x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
	Unit	umol/h/mg MP	umol/h/g liver	umol/h	umol/h/kg BW^0.75	mg/h/kg BW^0.75

Male Mouse	Values	0.085	20	**0.495**
LUNG	Scaling & calculation		x **MPPGLU (mg MP/g lung)**	x **BW (kg) X VLUC X 1000 (g/kg)**
	Unit	umol/h/mg MP	umol/h/g lung	umol/h

Biological Scaling	VmaxLUc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight
Female Rat	Values	0.0041	20	**0.104**
LUNG	Scaling & calculation		x **MPPGLU (mg MP/g lung)**	x **BW (kg) X VLUC X 1000 (g/kg)**
	Unit	umol/h/mg MP	umol/h/g lung	umol/h

5.53	0.49
/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
umol/h/kg BW^0.75	mg/h/kg BW^0.75

Male Mouse	Values	0.012	18	0.139
KIDNEY	Scaling & calculation		x MPPGK (mg MP/g kidney)	x BW (kg) x VKC x 1000 (g/kg)
	Unit	umol/h/mg MP	umol/h/g kidney	umol/h

/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
0.29	0.026
/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
umol/h/kg BW^0.75	mg/h/kg BW^0.75

Biological Scaling	VmaxKIDc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight
Female Rat	Values	0.0018	18	0.062
KIDNEY	Scaling & calculation		x MPPGK (mg MP/g kidney)	x BW (kg) x VKC x 1000 (g/kg)
	Unit	umol/h/mg MP	umol/h/g kidney	umol/h

Biological Scaling	VmaxKIDc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight
Male Rat	Values	0.0019	18	0.102
KIDNEY	Scaling & calculation		x MPPGK (mg MP/g kidney)	x BW (kg) x VKC x 1000 (g/kg)
	Unit	umol/h/mg MP	umol/h/g kidney	umol/h

1.56	0.14
/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
umol/h/kg BW^0.75	mg/h/kg BW^0.75

/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
0.17	0.015
/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
umol/h/kg BW^0.75	mg/h/kg BW^0.75

/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
0.20	0.018
/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
umol/h/kg BW^0.75	mg/h/kg BW^0.75

Biological Scaling	Vmaxc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight	/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
Mixed gender Human	Values	0.055	40	3965.37	163.86	14.51
LIVER	Scaling & calculation		x MPPGL (mg MP/g liver)	x BW (kg) x VLC x 1000 (g/kg)	/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
	Unit	umol/h/mg MP	umol/h/g liver	umol/h	umol/h/kg BW^0.75	mg/h/kg BW^0.75

Alternal Scaling

Biological Scaling	VmaxLUc (mg/h/kg BW^0.75)	In Vitro Value	x Scaling factor	x Tissue weight
Male Mouse	Values	7.88E-05	20	8.38E-01
LUNG	Scaling & calculation		x MPPGLU (mg MP/g lung)	x BW (kg) X VLUC X 1000 (g/kg)
	Unit	umol/h/mg MP	umol/h/g lung	umol/h

/BW^0.75	x MW = In vivo parameter (unit in PBPK model)
3.46E-02	3.07E-03
/BW^0.75	x MW (ug/umol)/1000 (ug/mg)
umol/h/kg BW^0.75	mg/h/kg BW^0.75

Uses IVIVE scaling approach from the Yoon report. (human lung Vmax calculated using approach from methylene chlorid

e - scaling liver in vitro vmax to lung based on ratio of ethoxycoumarin metabolism in lung to liver)

Dose metrics using parameters derived with MCMC estimate of

TSTOP **336 hrs** Amt. Metab. = mg/day/g tissue

Exposure: **6 hr/day 5 days/week**

Revised parameters from MCMC of In Vitro data with flux limitation included

Female Mouse Initial Parms				
ppm	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney	**Concentration Specific** BW (kg)
12.8	1.16	0.85	-	0.040
32	2.96	1.29	-	0.040
80	7.66	1.69	-	0.036

Amt. Metab. = mg/day/g tissue

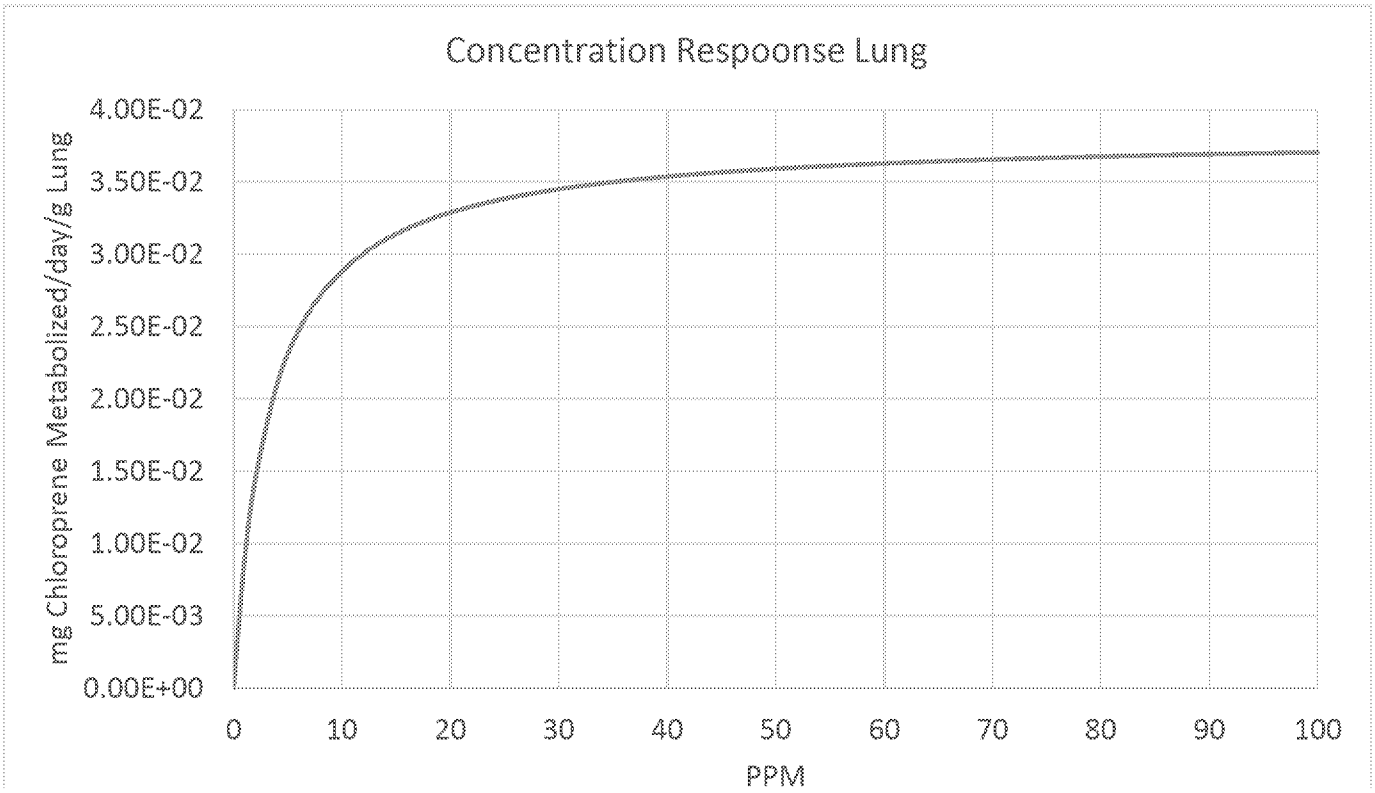
Human Initial Parms			
ppm	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney
12.8	0.30	0.0074	-
32	0.74	0.011	-
80	1.85	0.015	-

Amt. Metab. = mg/day/g tissue

Human Continuous Exposure (24 hr/day)

Human Parms Continuous Exposure			
PPM	Amt. Metab. Liver	Amt. Metab. Lung	Amt. Metab. Kidney
2.80E-04	**3.56E-05**	**3.24E-06**	-
1.00E-03	1.27E-04	1.16E-05	-
1.00E-02	1.27E-03	1.15E-04	-
1.00E-01	1.27E-02	1.12E-03	-
1.00E+00	1.28E-01	8.91E-03	-
2.00E+00	2.56E-01	1.45E-02	-
4.00E+00	5.13E-01	2.10E-02	-
6.00E+00	7.71E-01	2.47E-02	-
8.00E+00	1.03E+00	2.71E-02	-
1.00E+01	1.29E+00	2.88E-02	-
1.20E+01	1.54E+00	3.01E-02	-
1.40E+01	1.80E+00	3.10E-02	-
1.60E+01	2.06E+00	3.18E-02	-
1.80E+01	2.32E+00	3.24E-02	-
2.00E+01	2.58E+00	3.29E-02	-
2.20E+01	2.83E+00	3.33E-02	-
2.40E+01	3.09E+00	3.37E-02	-

f Kgl: 0.22 L/hr


Concentration Respoonse Lung
mg Chloroprene Metabolized/day/g Lung
4.00E-02
3.50E-02
3.00E-02
2.50E-02
2.00E-02
1.50E-02
1.00E-02
5.00E-03
0.00E+00
0
10
20
30
40
50
60
70
80
90
100
PPM

2.60E+01	3.35E+00	3.40E-02	-
2.80E+01	3.61E+00	3.43E-02	-
3.00E+01	3.87E+00	3.45E-02	-
3.20E+01	4.12E+00	3.47E-02	-
3.40E+01	4.38E+00	3.49E-02	-
3.60E+01	4.64E+00	3.51E-02	-
3.80E+01	4.90E+00	3.52E-02	-
4.00E+01	5.16E+00	3.54E-02	-
4.20E+01	5.41E+00	3.55E-02	-
4.40E+01	5.67E+00	3.56E-02	-
4.60E+01	5.93E+00	3.57E-02	-
4.80E+01	6.19E+00	3.58E-02	-
5.00E+01	6.45E+00	3.59E-02	-
5.20E+01	6.70E+00	3.60E-02	-
5.40E+01	6.96E+00	3.61E-02	-
5.60E+01	7.22E+00	3.61E-02	-
5.80E+01	7.48E+00	3.62E-02	-
6.00E+01	7.73E+00	3.63E-02	-
6.20E+01	7.99E+00	3.63E-02	-
6.40E+01	8.25E+00	3.64E-02	-
6.60E+01	8.51E+00	3.64E-02	-
6.80E+01	8.76E+00	3.65E-02	-
7.00E+01	9.02E+00	3.65E-02	-
7.20E+01	9.28E+00	3.66E-02	-
7.40E+01	9.54E+00	3.66E-02	-
7.60E+01	9.80E+00	3.67E-02	-
7.80E+01	1.01E+01	3.67E-02	-
8.00E+01	1.03E+01	3.67E-02	-
8.20E+01	1.06E+01	3.68E-02	-
8.40E+01	1.08E+01	3.68E-02	-
8.60E+01	1.11E+01	3.68E-02	-
8.80E+01	1.13E+01	3.69E-02	-
9.00E+01	1.16E+01	3.69E-02	-
9.20E+01	1.19E+01	3.69E-02	-
9.40E+01	1.21E+01	3.70E-02	-
9.60E+01	1.24E+01	3.70E-02	-
9.80E+01	1.26E+01	3.70E-02	-
1.00E+02	1.29E+01	3.70E-02	-