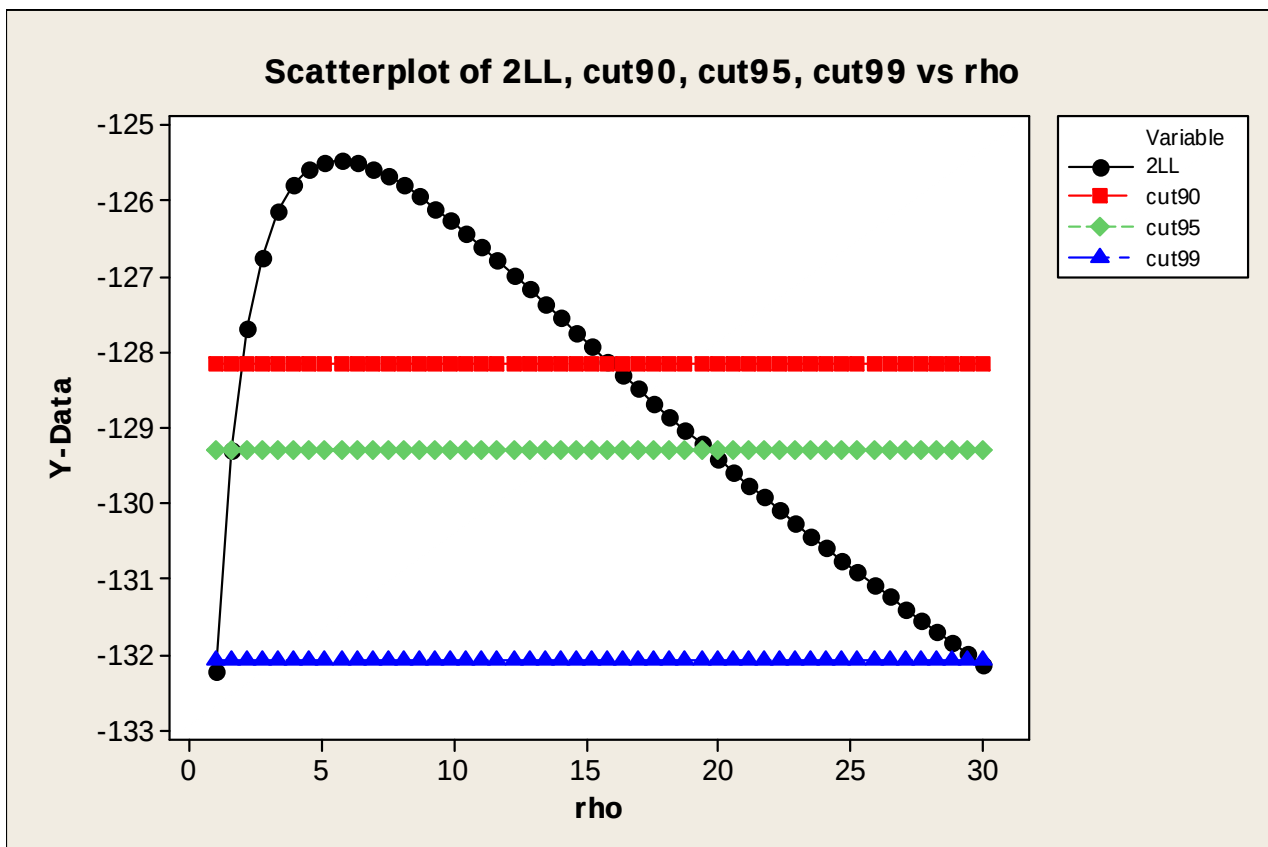
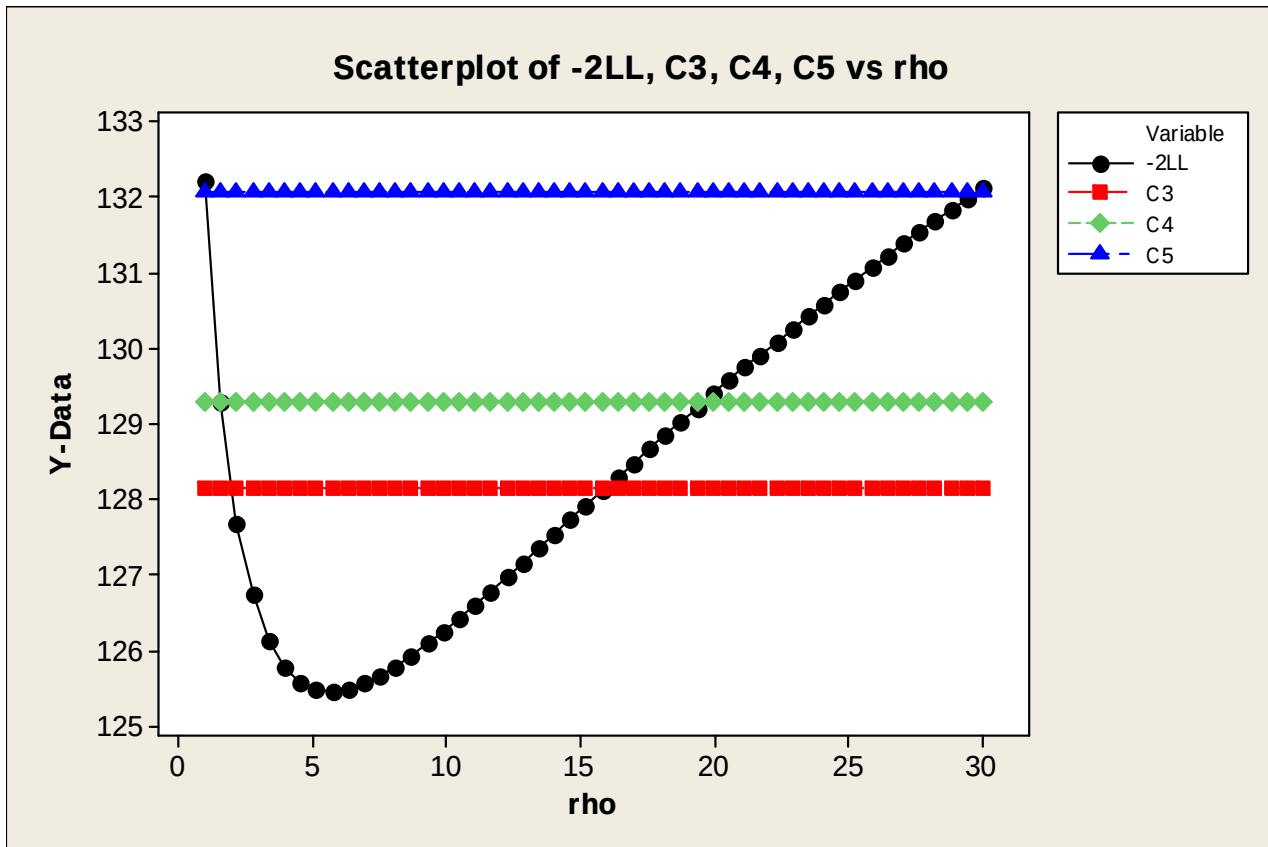
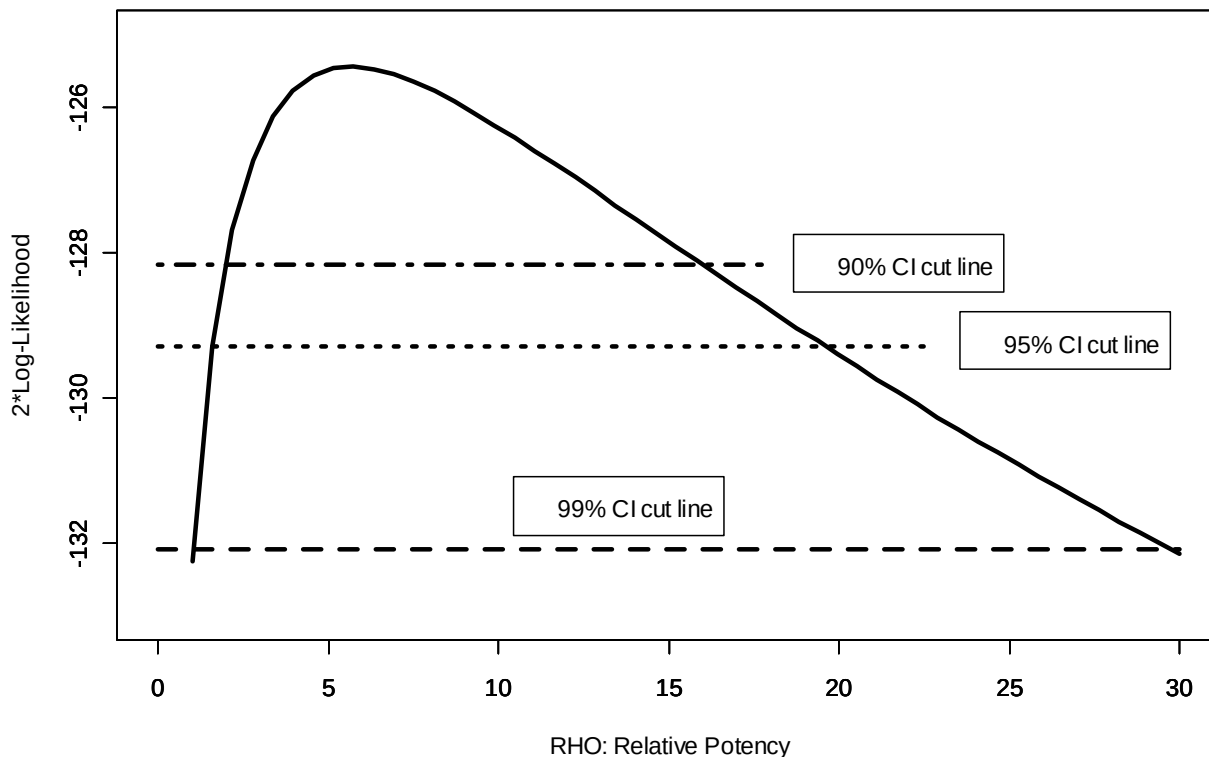


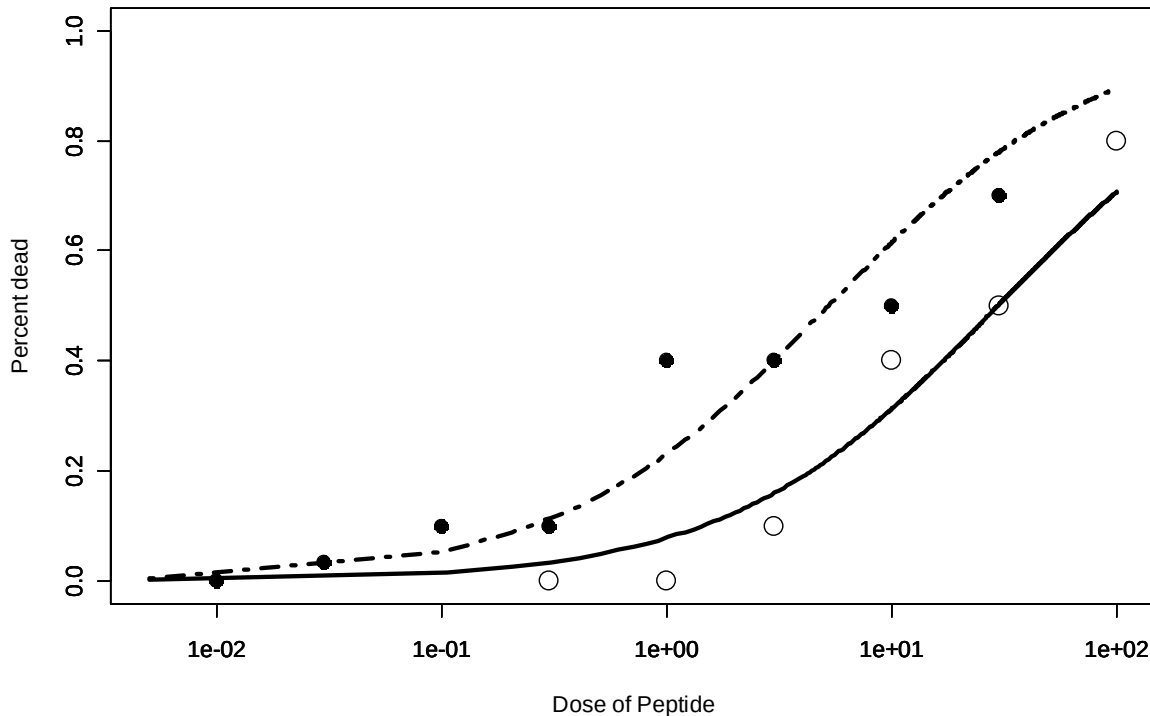




```

rho<-seq(1,30,length=50)
TwoLL<-c(-132.238,-129.302,-127.690,-126.728,-126.138,-125.780,-125.575,-125.476,-125.452,-125.483,
-125.555,-125.658,-125.783,-125.926,-126.082,-126.248,-126.422,-126.602,-126.785,-126.972,
-127.160,-127.350,-127.540,-127.731,-127.921,-128.110,-128.298,-128.485,-128.670,-128.854,
-129.037,-129.217,-129.396,-129.573,-129.748,-129.921,-130.093,-130.262,-130.429,-130.595,
-130.758,-130.920,-131.080,-131.238,-131.394,-131.548,-131.700,-131.851,-132.000,-132.147)
cut90<-rep(-128.162,50)
cut95<-rep(-129.292,50)
cut99<-rep(-132.082,50)
xrange<-range(0,30)
yrange<-range(-133,-125)
rhoa<-seq(0,18,length=50)
rhob<-seq(0,22.5,length=50)
rhoc<-seq(0,30,length=50)
plot(rho,TwoLL,type="l",lwd=3,xlim=xrange,ylim=yrange,xlab="RHO: Relative Potency",ylab="2*Log-Likelihood")
par(new=T)
plot(rhoa,cut90,type="l",lwd=3,xlim=xrange,ylim=yrange,xlab="",ylab="",lty=4)
par(new=T)
plot(rhob,cut95,type="l",lwd=3,xlim=xrange,ylim=yrange,xlab="",ylab="",lty=3)
par(new=T)
plot(rhoc,cut99,type="l",lwd=3,xlim=xrange,ylim=yrange,xlab="",ylab="",lty=2)
legend(locator(1),legend=c("99% CI cut line"))
legend(locator(1),legend=c("95% CI cut line"))
legend(locator(1),legend=c("90% CI cut line"))

```



```

pi.for.LL2<-function(x,th2,th3) {
  t<-(x/th2)^th3
  den<-1+t
  t/den }
dose<-seq(0.005,100,length=1000)
pi.s<-pi.for.LL2(dose,29.4724,0.7234)
pi.n<-pi.for.LL2(dose,5.2035,0.7234)
xrange<-range(0.005,100)
yrange<-range(0,1)
n.dose<-c(0.01,0.03,0.1,0.3,1,3,10,30)
n.y<-c(0,1,1,1,4,4,5,7)
n.n<-c(30,30,10,10,10,10,10,10)
n.pct<-n.y/n.n
s.dose<-c(0.30,1,3,10,30,100)
s.y<-c(0,0,1,4,5,8)
s.n<-c(10,10,10,10,10,10)
s.pct<-s.y/s.n
plot(dose,pi.s,type="l",lwd=3,xlim=xrange,ylim=yrange,xlab="Dose of Peptide",ylab="Percent dead",
log="x")
par(new=T)
plot(dose,pi.n,type="l",lwd=3,xlim=xrange,ylim=yrange,xlab="",ylab="",log="x",lty=4)
par(new=T)
plot(s.dose,s.pct,xlim=xrange,ylim=yrange,xlab="",ylab="",cex=2,log="x")
par(new=T)
plot(n.dose,n.pct,xlim=xrange,ylim=yrange,xlab="",ylab="",cex=2,pch=20,log="x")

```

Full Model (after retaining parallelism):

```
proc nlmixed;
  parms rho=1 th2N=2 th3=1;
  th2=rho*th2N*S_Peptide+th2N*N_Peptide;
  t=(dose/th2)**th3; p=t/(1+t);
  model y~binomial(n,p);
run;
```

The NLMIXED Procedure								
Fit Statistics								
-2 Log Likelihood							33.4	
AIC (smaller is better)							39.4	
AICC (smaller is better)							41.8	
BIC (smaller is better)							41.4	
Parameter Estimates								
	Standard							
Parameter	Estimate	Error	DF	t Value	Pr > t	Alpha	Lower	Upper
rho	5.6639	3.5241	14	1.61	0.1303	0.05	-1.8946	13.2224
th2N	5.2036	2.3301	14	2.23	0.0424	0.05	0.2060	10.2011
th3	0.7234	0.1177	14	6.15	<.0001	0.05	0.4709	0.9759

Reduced Model (after imposing the Null Hypothesis)

```
proc nlmixed;
  parms th2N=2 th3=1; rho=1;
  th2=rho*th2N*S_Peptide+th2N*N_Peptide;
  t=(dose/th2)**th3; p=t/(1+t);
  model y~binomial(n,p);
run;
```

The NLMIXED Procedure								
Fit Statistics								
-2 Log Likelihood							40.2	
AIC (smaller is better)							44.2	
AICC (smaller is better)							45.3	
BIC (smaller is better)							45.5	
Parameter Estimates								
Parameter	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
th2N	14.0797	5.6074	14	2.51	0.0249	0.05	2.0530	26.1065
th3	0.6138	0.1047	14	5.86	<.0001	0.05	0.3893	0.8384

$\chi_1^2 = 40.2 - 33.4 = 6.8$, p-value: (R code) "1-pchisq(6.8,1)" (R result) "0.009115787"

This demonstrates that $p < 0.01$, which is what we discerned by looking at the plots on pp.1-2 above and noticing that the vertical line at $x = 1$ hits the curve just outside of the 99% PLCI.