* 1. **R Code from linear fits**

**R Code and Results from linear fits of 2, 3 and 4 parameter models**

library(boot)

dataset<-read.csv("Tambjamines\_New\_numbers\_classified\_cleaned.csv")
ds.sb<-dataset[,c('ï..Compound.no','Ring.substituent', 'NH.substituent','Enamine.Substituent','R.type','Log.1.EC50.','ALOGPs','ALOGPs.sq','nH','Mv','J3D','AMW','J','ARR','nCIC','Polarizability..cm3.')]

plot(ds.sb$ALOGPs, ds.sb$Log.1.EC50., main="Simple plot of Log(1/EC50) against ALOGPs", xlab="ALOGPs", ylab="Log(1/EC50)")
#plots ALOGPs against log(1/ec50)

# define stats function to give to boot strap, at this stage just the quadratic fit
bs <- function(formula, data, indices) {
d <- data[indices,] # allows boot to select sample
fit <- lm(formula, data=d)
return(coef(fit))
}

# define simpler data frame and give x and y variables
# gives dataframe with only 2 columns (the necessary columns)
df1 <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50.)

# define the strata
# limits of ALOGPs are below 1.5 and above 6 in this set
strata <- ifelse(ds.sb$ALOGPs > 1.5, 1,0)+ ifelse(ds.sb$ALOGPs > 6, 1,0)

**#ALOGPs, ALOGPS-sq**

# do the bootstrap
res\_plainfit <-boot(data = df1, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2))

# now evaluate the confidence limit from the boot strap, index = 1 is the intercept, 2 the
# coefficient of ALOGPs and 3 the coefficient of ALOGPs^2
# bca - Adjusted Bootstrap percentile interval

> boot.ci(res\_plainfit, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_plainfit, type = "bca", index = 1)

Intervals :

Level BCa

95% (-1.1079, -0.0859 )

Calculations and Intervals on Original Scale

> boot.ci(res\_plainfit, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_plainfit, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 0.904, 1.470 )

Calculations and Intervals on Original Scale

> boot.ci(res\_plainfit, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_plainfit, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.1658, -0.0926 )

Calculations and Intervals on Original Scale

# do the usual linear least squares for the quadratic
# lm is linear model using df1 as the data source
fitplain <- lm(y ~ x + I(x^2), data = df1)

# look at the coefficients and confidence limit from the least squares

> summary(fitplain)

Call:

lm(formula = y ~ x + I(x^2), data = df1)

Residuals:

 Min 1Q Median 3Q Max

-0.71723 -0.17356 0.02163 0.25389 0.49909

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) -0.57873 0.29008 -1.995 0.0529 .

x 1.20333 0.14861 8.097 5.83e-10 \*\*\*

I(x^2) -0.13293 0.01746 -7.613 2.67e-09 \*\*\*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.3056 on 40 degrees of freedom

Multiple R-squared: 0.6292, Adjusted R-squared: 0.6106

F-statistic: 33.93 on 2 and 40 DF, p-value: 2.42e-09confint(fitplain)
2.5 % 97.5 %
(Intercept) -1.1829892 -0.008978968
x 0.9142820 1.515710944
I(x^2) -0.1699811 -0.099315781
>

> confint(fitplain)

 2.5 % 97.5 %

(Intercept) -1.1650147 0.00754727

x 0.9029908 1.50367778

I(x^2) -0.1682162 -0.09763807

**#ALOGPs, ALOGPs-sq, nH**

# now extend to include nH

dfnH <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$nH)

# usual least square fit and estimates

fitnH <- lm(y ~ x + I(x^2) + z, data = dfnH)

> summary(fitnH)

Call:

lm(formula = y ~ x + I(x^2) + z, data = dfnH)

Residuals:

 Min 1Q Median 3Q Max

-0.52009 -0.12461 -0.02989 0.14692 0.54953

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) -1.65858 0.30541 -5.431 3.19e-06 \*\*\*

x 1.30991 0.11713 11.183 9.83e-14 \*\*\*

I(x^2) -0.17580 0.01584 -11.101 1.23e-13 \*\*\*

z 0.06525 0.01247 5.233 5.98e-06 \*\*\*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2372 on 39 degrees of freedom

Multiple R-squared: 0.7822, Adjusted R-squared: 0.7654

F-statistic: 46.67 on 3 and 39 DF, p-value: 5.615e-13

> confint(fitnH)

 2.5 % 97.5 %

(Intercept) -2.27633322 -1.0408314

x 1.07298335 1.5468355

I(x^2) -0.20783293 -0.1437676

z 0.04002894 0.0904637

# now bootstrap

res\_fitnH <-boot(data = dfnH, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z)

#res\_fitnH is including nH

# look at confidence intervals (now seem a little different to above)

#uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - nH

> boot.ci(res\_fitnH, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH, type = "bca", index = 1)

Intervals :

Level BCa

95% (-2.454, -1.033 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnH, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.038, 1.601 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnH, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.2132, -0.1302 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnH, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH, type = "bca", index = 4)

Intervals :

Level BCa

95% ( 0.0433, 0.0874 )

Calculations and Intervals on Original Scale

**#ALOGPs, ALOGPs-sq, Mv**

# now extend to include Mv

dfMv <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$Mv)

# usual least square fit and estimates

fitMv <- lm(y ~ x + I(x^2) + z, data = dfMv)

#lines(ds.sb$ALOGPs[ord],fitted(fitMv)[ord],col="green")

summary(fitMv)

Call: lm(formula = y ~ x + I(x^2) + z, data = dfMv)

Residuals:

 Min 1Q Median 3Q Max

-0.62519 -0.09623 -0.00267 0.10307 0.50699

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) 3.36237 0.75384 4.460 6.76e-05 \*\*\*

x 1.37214 0.11736 11.692 2.56e-14 \*\*\*

I(x^2) -0.15793 0.01407 -11.227 8.75e-14 \*\*\*

z -6.61570 1.20981 -5.468 2.83e-06 \*\*\*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2328 on 39 degrees of freedom

Multiple R-squared: 0.7901, Adjusted R-squared: 0.774

F-statistic: 48.93 on 3 and 39 DF, p-value: 2.732e-13

confint(fitMv)

 2.5 % 97.5 %

(Intercept) 1.8375883 4.8871494

x 1.1347599 1.6095207

I(x^2) -0.1863835 -0.1294758

z -9.0627723 -4.1686238

# now bootstrap

res\_fitMv <-boot(data = dfMv, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z)

#res\_fitMv is including Mv

#uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - Mv

> boot.ci(res\_fitMv, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitMv, type = "bca", index = 1)

Intervals :

Level BCa

95% ( 2.159, 4.419 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitMv, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitMv, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.126, 1.579 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitMv, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitMv, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.1895, -0.1229 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitMv, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitMv, type = "bca", index = 4)

Intervals :

Level BCa

95% (-8.432, -4.473 )

Calculations and Intervals on Original Scale

**#ALOGPs, ALOGPs-sq, J3D**

# now extend to include J3D

dfJ3D <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$J3D)

# usual least square fit and estimates

fitJ3D <- lm(y ~ x + I(x^2) + z, data = dfJ3D)

#lines(ds.sb$ALOGPs[ord],fitted(fitJ3D)[ord],col="green")

> summary(fitJ3D)

Call: lm(formula = y ~ x + I(x^2) + z, data = dfJ3D)

Residuals:

 Min 1Q Median 3Q Max

-0.60320 -0.11738 0.00310 0.09931 0.49719

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) -2.3723 0.3971 -5.973 5.64e-07 \*\*\*

x 1.3394 0.1162 11.527 3.94e-14 \*\*\*

I(x^2) -0.1476 0.0136 -10.850 2.42e-13 \*\*\*

z 0.7332 0.1348 5.441 3.09e-06 \*\*\*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2333 on 39 degrees of freedom

Multiple R-squared: 0.7892, Adjusted R-squared: 0.773

F-statistic: 48.67 on 3 and 39 DF, p-value: 2.971e-13

> confint(fitJ3D)

 2.5 % 97.5 %

(Intercept) -3.1755219 -1.5689714

x 1.1043710 1.5744203

I(x^2) -0.1750866 -0.1200634

z 0.4606703 1.0058329

# now bootstrap

res\_fitJ3D <-boot(data = dfJ3D, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z)

#res\_fitJ3D is including J3D

# look at confidence intervals (now seem a little different to above)

#uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - J3D

> boot.ci(res\_fitJ3D, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitJ3D, type = "bca", index = 1)

Intervals :

Level BCa

95% (-3.071, -1.648 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitJ3D, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitJ3D, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.109, 1.556 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitJ3D, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitJ3D, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.1770, -0.1145 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitJ3D, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitJ3D, type = "bca", index = 4)

Intervals :

Level BCa

95% ( 0.4952, 0.9602 )

Calculations and Intervals on Original Scale

>

**#ALOGPs, ALOGPs-sq, ARR**

# now extend to include ARR

dfARR <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$ARR)

# usual least square fit and estimates

fitARR <- lm(y ~ x + I(x^2) + z, data = dfARR)

> summary(fitARR)

Call: lm(formula = y ~ x + I(x^2) + z, data = dfARR)

Residuals:

 Min 1Q Median 3Q Max

-0.65423 -0.09241 0.00022 0.10878 0.51673

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) -0.22238 0.24537 -0.906 0.37

x 1.36602 0.12449 10.973 1.73e-13 \*\*\*

I(x^2) -0.15271 0.01467 -10.412 8.05e-13 \*\*\*

z -1.67499 0.35198 -4.759 2.67e-05 \*\*\*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2461 on 39 degrees of freedom

Multiple R-squared: 0.7654, Adjusted R-squared: 0.7473

F-statistic: 42.41 on 3 and 39 DF, p-value: 2.358e-12

> confint(fitARR)

 2.5 % 97.5 %

(Intercept) -0.7186996 0.2739332

x 1.1142092 1.6178228

I(x^2) -0.1823700 -0.1230402

z -2.3869397 -0.9630480

# now bootstrap

res\_fitARR <-boot(data = dfARR, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z)

#res\_fitARR is including ARR

# look at confidence intervals (now seem a little different to above)

#uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - ARR

> boot.ci(res\_fitARR, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitARR, type = "bca", index = 1)

Intervals :

Level BCa

95% (-0.6466, 0.0697 )

Calculations and Intervals on Original Scale

Some BCa intervals may be unstable

> boot.ci(res\_fitARR, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitARR, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.117, 1.605 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitARR, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitARR, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.1863, -0.1160 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitARR, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitARR, type = "bca", index = 4)

Intervals :

Level BCa

95% (-2.290, -1.065 )

Calculations and Intervals on Original Scale

**#ALOGPs, ALOGPs-sq, AMW**

# now extend to include AMW

dfAMW <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$AMW)

# usual least square fit and estimates

fitAMW <- lm(y ~ x + I(x^2) + z, data = dfAMW)

> summary(fitAMW)

Call: lm(formula = y ~ x + I(x^2) + z, data = dfAMW)

Residuals:

 Min 1Q Median 3Q Max

-0.61861 -0.12959 0.02152 0.15637 0.41613

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) 0.73091 0.34409 2.124 0.04 \*

x 1.33046 0.11940 11.143 1.09e-13 \*\*\*

I(x^2) -0.15404 0.01433 -10.747 3.20e-13 \*\*\*

z -0.19952 0.03928 -5.080 9.72e-06 \*\*\*

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Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2401 on 39 degrees of freedom

Multiple R-squared: 0.7768, Adjusted R-squared: 0.7597

F-statistic: 45.25 on 3 and 39 DF, p-value: 8.955e-13

> confint(fitAMW)

 2.5 % 97.5 %

(Intercept) 0.03492571 1.4268963

x 1.08895355 1.5719752

I(x^2) -0.18302806 -0.1250454

z -0.27896332 -0.1200808

# now bootstrap

res\_fitAMW <-boot(data = dfAMW, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z)

#res\_fitAMW is including AMW

# look at confidence intervals (now seem a little different to above)

#uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - AMW

> boot.ci(res\_fitAMW, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW, type = "bca", index = 1)

Intervals :

Level BCa

95% (-0.1126, 1.3684 )

Calculations and Intervals on Original Scale

Some BCa intervals may be unstable

> boot.ci(res\_fitAMW, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.104, 1.536 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitAMW, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.1820, -0.1212 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitAMW, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW, type = "bca", index = 4)

Intervals :

Level BCa

95% (-0.2931, -0.1331 )

Calculations and Intervals on Original Scale

Some BCa intervals may be unstable

**#ALOGPS, ALOGPs-sq, nCIC, J3D**

#ALogPs, ALogPs^2, nCIC, J3D

dfnCIC\_J3D <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$nCIC, w=ds.sb$J3D)

# usual least square fit and estimates

fitnCIC\_J3D <- lm(y ~ x + I(x^2) + z + w, data = dfnCIC\_J3D)

> summary(fitnCIC\_J3D)

Call: lm(formula = y ~ x + I(x^2) + z + w, data = dfnCIC\_J3D)

Residuals:

 Min 1Q Median 3Q Max

-0.49204 -0.14596 0.03286 0.09284 0.47415

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) -5.1054 1.2220 -4.178 0.000166 \*\*\*

x 1.2837 0.1125 11.409 7.73e-14 \*\*\*

I(x^2) -0.1457 0.0129 -11.295 1.04e-13 \*\*\*

z 0.4105 0.1746 2.351 0.024036 \*

w 1.5873 0.3851 4.122 0.000196 \*\*\*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2209 on 38 degrees of freedom

Multiple R-squared: 0.816, Adjusted R-squared: 0.7966

F-statistic: 42.12 on 4 and 38 DF, p-value: 1.784e-13

> confint(fitnCIC\_J3D)

 2.5 % 97.5 %

(Intercept) -7.57929116 -2.6315691

x 1.05592808 1.5114640

I(x^2) -0.17181680 -0.1195890

z 0.05696876 0.7640868

w 0.80774675 2.3668022

# now bootstrap

res\_fitnCIC\_J3D <-boot(data = dfnCIC\_J3D, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z +w)

#res\_fitnCIC\_J3D is including nCIC\_J3D

# look at confidence intervals - uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - nCIC

# index 5 - J3D

> boot.ci(res\_fitnCIC\_J3D, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnCIC\_J3D, type = "bca", index = 1)

Intervals :

Level BCa

95% (-7.681, -2.694 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnCIC\_J3D, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnCIC\_J3D, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.087, 1.493 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnCIC\_J3D, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnCIC\_J3D, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.1730, -0.1161 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnCIC\_J3D, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnCIC\_J3D, type = "bca", index = 4)

Intervals :

Level BCa

95% ( 0.0638, 0.7957 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnCIC\_J3D, type="bca",index=5)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnCIC\_J3D, type = "bca", index = 5)

Intervals :

Level BCa

95% ( 0.796, 2.330 )

Calculations and Intervals on Original Scale

**#ALOGPs, ALOGPs-sq, AMW, J3D**

#ALogPs, ALogPs^2, AMW, J3D

dfAMW\_J3D <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$AMW, w=ds.sb$J3D)

# usual least square fit and estimates

fitAMW\_J3D <- lm(y ~ x + I(x^2) + z + w, data = dfAMW\_J3D)

> summary(fitAMW\_J3D)

Call: lm(formula = y ~ x + I(x^2) + z + w, data = dfAMW\_J3D)

Residuals:

 Min 1Q Median 3Q Max

-0.58907 -0.10352 0.01421 0.08473 0.47939

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) -1.01799 0.70868 -1.436 0.15905

x 1.36148 0.11096 12.270 8.67e-15 \*\*\*

I(x^2) -0.15404 0.01325 -11.625 4.43e-14 \*\*\*

z -0.10996 0.04868 -2.259 0.02973 \*

w 0.47467 0.17187 2.762 0.00881 \*\*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2219 on 38 degrees of freedom

Multiple R-squared: 0.8141, Adjusted R-squared: 0.7946

F-statistic: 41.61 on 4 and 38 DF, p-value: 2.144e-13

> confint(fitAMW\_J3D)

 2.5 % 97.5 %

(Intercept) -2.4526500 0.41666156

x 1.1368500 1.58610083

I(x^2) -0.1808690 -0.12721712

z -0.2085162 -0.01140107

w 0.1267242 0.82260733

# now bootstrap

res\_fitAMW\_J3D <-boot(data = dfAMW\_J3D, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z +w)

#res\_fitAMW\_J3D is including AMW\_J3D

# look at confidence intervals - uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - AMW

# index 5 - J3D

> boot.ci(res\_fitAMW\_J3D, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW\_J3D, type = "bca", index = 1)

Intervals :

Level BCa

95% (-2.309, 0.429 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitAMW\_J3D, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW\_J3D, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.123, 1.591 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitAMW\_J3D, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW\_J3D, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.1852, -0.1194 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitAMW\_J3D, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW\_J3D, type = "bca", index = 4)

Intervals :

Level BCa

95% (-0.2182, -0.0512 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitAMW\_J3D, type="bca",index=5)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitAMW\_J3D, type = "bca", index = 5)

Intervals :

Level BCa

95% ( 0.1479, 0.7805 )

Calculations and Intervals on Original Scale

**#ALOGPs, ALOGPs-sq, nH, J**

#ALogPs, ALogPs^2, nH, J

dfnH\_J <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$nH, w=ds.sb$J)

# usual least square fit and estimates

fitnH\_J <- lm(y ~ x + I(x^2) + z + w, data = dfnH\_J)

> summary(fitnH\_J)

Call: lm(formula = y ~ x + I(x^2) + z + w, data = dfnH\_J)

Residuals:

 Min 1Q Median 3Q Max

-0.51391 -0.10098 -0.02125 0.07999 0.54360

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) -3.06707 0.61117 -5.018 1.25e-05 \*\*\*

x 1.43233 0.11898 12.039 1.55e-14 \*\*\*

I(x^2) -0.17239 0.01484 -11.620 4.49e-14 \*\*\*

z 0.04414 0.01418 3.113 0.00351 \*\*

w 0.90448 0.34719 2.605 0.01304 \*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2213 on 38 degrees of freedom

Multiple R-squared: 0.8152, Adjusted R-squared: 0.7957

F-statistic: 41.9 on 4 and 38 DF, p-value: 1.933e-13

> confint(fitnH\_J)

 2.5 % 97.5 %

(Intercept) -4.30432090 -1.82982567

x 1.19146973 1.67318501

I(x^2) -0.20242439 -0.14235652

z 0.01543404 0.07283738

w 0.20163869 1.60732816

>

# now bootstrap

res\_fitnH\_J <-boot(data = dfnH\_J, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z +w)

#res\_fitnH\_J is including nH\_J

# look at confidence intervals - uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - nH

# index 5 - J

> boot.ci(res\_fitnH\_J, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH\_J, type = "bca", index = 1)

Intervals :

Level BCa

95% (-4.133, -1.767 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnH\_J, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH\_J, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.196, 1.653 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnH\_J, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH\_J, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.2047, -0.1278 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnH\_J, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH\_J, type = "bca", index = 4)

Intervals :

Level BCa

95% ( 0.0139, 0.0705 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitnH\_J, type="bca",index=5)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitnH\_J, type = "bca", index = 5)

Intervals :

Level BCa

95% ( 0.1729, 1.4745 )

Calculations and Intervals on Original Scale

**#ALOGPs, ALOGPs-sq, Polarizability, nH**

#ALogPs, ALogPs^2, Polarizability..cm3., nH

dfPol\_nH <-data.frame(x=ds.sb$ALOGPs,y=ds.sb$Log.1.EC50., z=ds.sb$Polarizability..cm3., w=ds.sb$nH)

# usual least square fit and estimates

fitPol\_nH <- lm(y ~ x + I(x^2) + z + w, data = dfPol\_nH)

> summary(fitPol\_nH)

Call: lm(formula = y ~ x + I(x^2) + z + w, data = dfPol\_nH)

Residuals:

 Min 1Q Median 3Q Max

-0.57511 -0.10224 -0.02149 0.08645 0.58694

Coefficients:

 Estimate Std. Error t value Pr(>|t|)

(Intercept) -0.983048 0.414418 -2.372 0.0229 \*

x 1.306968 0.111287 11.744 3.26e-14 \*\*\*

I(x^2) -0.164507 0.015837 -10.387 1.18e-12 \*\*\*

z -0.021601 0.009462 -2.283 0.0281 \*

w 0.062608 0.011900 5.261 5.86e-06 \*\*\*

---

Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 0.2253 on 38 degrees of freedom

Multiple R-squared: 0.8084, Adjusted R-squared: 0.7883

F-statistic: 40.09 on 4 and 38 DF, p-value: 3.786e-13

> confint(fitPol\_nH)

 2.5 % 97.5 %

(Intercept) -1.82199334 -0.144102492

x 1.08167950 1.532255543

I(x^2) -0.19656852 -0.132446274

z -0.04075559 -0.002446523

w 0.03851716 0.086699013

fitPol\_nH\_pred<-fitted(fitPol\_nH) #predicted values of fit3

# plot(fitPol\_nH, dfPol\_nH$y, main="fitPol\_nH predicted vs actual") # plots predicted vs actual values

# now bootstrap

res\_fitPol\_nH <-boot(data = dfPol\_nH, statistic = bs, strata = strata, R=999, formula = y ~ x + I(x^2)+z +w)

#res\_fitPol\_nH is including Pol\_nH

# look at confidence intervals - uses the bootstrap function

# index 1 - intercept?

# index 2 - ALOGPs

# index 3 - ALOGPs^2

# index 4 - Molec.Volume..cm3.

# index 5 - nH

> boot.ci(res\_fitPol\_nH, type="bca",index=1)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitPol\_nH, type = "bca", index = 1)

Intervals :

Level BCa

95% (-1.7356, 0.0784 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitPol\_nH, type="bca",index=2)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitPol\_nH, type = "bca", index = 2)

Intervals :

Level BCa

95% ( 1.032, 1.519 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitPol\_nH, type="bca",index=3)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitPol\_nH, type = "bca", index = 3)

Intervals :

Level BCa

95% (-0.1990, -0.1102 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitPol\_nH, type="bca",index=4)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitPol\_nH, type = "bca", index = 4)

Intervals :

Level BCa

95% (-0.0363, 0.0050 )

Calculations and Intervals on Original Scale

> boot.ci(res\_fitPol\_nH, type="bca",index=5)

BOOTSTRAP CONFIDENCE INTERVAL CALCULATIONS

Based on 999 bootstrap replicates

CALL :

boot.ci(boot.out = res\_fitPol\_nH, type = "bca", index = 5)

Intervals :

Level BCa

95% ( 0.0399, 0.0865 )

Calculations and Intervals on Original Scale

>