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# Homework 2

**BME 7410**

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### 3.8 Problem regarding Silicosis:

Here,

n= number of mice=23;

u = mean MIP-2 expression level = 11.4 pg/mL;

sigma = standard deviation of the MIP-2 expression level = 5.75

**a)** We know that,

$$\begin{aligned}\text{Standard error of the mean} &= \frac{\sigma}{\sqrt{n}} \\ &= \frac{11.4 \text{ pg/mL}}{\sqrt{23}} \\ &= 2.377 \text{ pg/mL}\end{aligned}$$

**b)** For normally distributed variables, 95% confidence interval is:

mean-2\*sigma to mean +2\*sigma

= 11.4 – 2\*5.75 , 11.4 + 2\*5.75

= -0.1 , 22.9

### 3.14 Error propagation in cell diameter

Here,

$$V = \text{Cell volume} = 623.6 \pm 289.1 \text{ } \mu\text{m}^3$$

$$\text{So, } \bar{V} = \text{mean volume} = 623.6 \text{ } \mu\text{m}^3$$

and, standard deviation volume,  $S_V = 289.1$

If cell diameter is denoted by  $d$ , the relation between  $d$  and  $V$  is,

$$d = \left( \frac{6 \cdot V}{\pi} \right)^{\frac{1}{3}}$$

if  $z = f(x)$ , according to error propagation formulas,

$$\bar{z} = \text{mean}(z) = f(\bar{x}) \text{ where } \bar{x} \text{ is mean of independent variable}$$

$$\text{and, } s_z = \text{standard deviation}(z) = s_x * \left( \frac{\partial f}{\partial x} \text{ at } \bar{x} \right)$$

$$\begin{aligned} \text{Now, mean diameter, } \bar{d} &= \left( \frac{6 \cdot \bar{V}}{\pi} \right)^{\frac{1}{3}} \\ &= \left( \frac{6 \cdot 623.6}{\pi} \right)^{\frac{1}{3}} \text{ } \mu\text{m} \\ &= 10.6 \text{ } \mu\text{m} \end{aligned}$$

$$\text{And, standard deviation of diameter, } S_d = S_V * \left\{ \frac{1}{3} * \left( \frac{6 \cdot \bar{V}}{\pi} \right)^{\frac{-2}{3}} * \frac{6}{\pi} \right\}$$

$$\begin{aligned} &= S_V * \left\{ \frac{1}{3} * \left( \frac{6 \cdot \bar{V}}{\pi} \right)^{\frac{-2}{3}} * \frac{6}{\pi} \right\} \\ &= 289.1 * \left\{ \frac{1}{3} * \left( \frac{6 \cdot 623.6}{\pi} \right)^{\frac{-2}{3}} * \frac{6}{\pi} \right\} \\ &= 1.64 \end{aligned}$$

### 3.16 Reaction Rate Problem

Michaelis-Menten kinetics of enzyme reaction is described by the following equation:

$$\frac{1}{R} = \frac{1}{R_{max}} + \frac{K_m}{R_{max}} * \frac{1}{S}$$

Or,  $Y = c + m * X$

Where,  $Y = \frac{1}{R}$  (R is the reaction rate in concentration/time);

$X = \frac{1}{S}$  (S is the substrate concentration);

$m = \frac{K_m}{R_{max}}$  and  $c = \frac{1}{R_{max}}$  ( $R_{max}$  is the maximum reaction rate for a particular enzyme concentration,  $K_m$  is the Michaelis constant)

Here, we have DOG conc. Data and corresponding reaction rate with or without progesterone. Without progesterone, we have two data points missing. So, we perform calculations with eight data points for with progesterone reaction rate and with six data points for without progesterone rate.

#### Matlab Script:

```
%Reaction Rate fitting problem
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% R is the reaction rate in concentration/time;  
% S is the substrate concentration;
```

```
%matrix of modeling functions: first column of ones, second column =  
1/S,  
%output is 1/R  
%We shall denote our model by the vector equation  $A*x=b$ 
```

```
%DOG data points for reaction rate with progesterone  
A1=[ones(1,8); 1/5 1/10 1/20 1/25 1/30 1/40 1/50 1/60]';
```

%DOG data points for reaction rate with progesterone

A2=[ones(1,6); 1/5 1/10 1/25 1/30 1/40 1/60]';

%Reaction rates with progesterone

Y1=[1/3.25 1/2.4 1/5.1 1/6 1/7.2 1/7.7 1/9.1 1/9.05]';

%Reaction rates without progesterone

Y2=[1/2.4 1/3.75 1/4.05 1/5.4 1/6.5 1/7.8]';

%calculating K for both cases

K1=inv(A1'\*A1)\*A1';

K2=inv(A2'\*A2)\*A2';

%our modeling parameters, (1/Rmax, Km/Rmax)

%calculating modeling parameters for both cases

x1=K1\*Y1;

x2=K2\*Y2;

%variance in data

Shsq1=sum((Y1-A1\*x1).^2)/(8-2);

Shsq2=sum((Y2-A2\*x2).^2)/(6-2);

%variance in modeling parameter

Sx1sq1=K1(1,:)\*K1(1,:)'\*Shsq1;

Sx2sq1=K1(2,:)\*K1(2,:)'\*Shsq1;

Sx1sq2=K2(1,:)\*K2(1,:)'\*Shsq2;

Sx2sq2=K2(2,:)\*K2(2,:)'\*Shsq2;

%covariances

S1x1x2 = Shsq1\*sum(K1(1,:).\*K1(2,:));

S2x1x2 = Shsq2\*sum(K2(1,:).\*K2(2,:));

%Kms

Km1 = x1(2)/x1(1);

Km2 = x2(2)/x2(1);

%Rmaxs

Rmax1 = 1/x1(1);

Rmax2 = 1/x2(1);

%standard deviation for Rmax

SRmax1 = (Rmax1/x1(1))\*sqrt(Sx1sq1);

SRmax2 = (Rmax2/x2(1))\*sqrt(Sx1sq2);

%standard deviation for Km

```

Skm1 = Km1*sqrt(Sx1sq1/x1(1).^2 + Sx2sq1/x1(2).^2 - 2*
S1x1x2/(x1(1)*x1(2)));
Skm2 = Km2*sqrt(Sx1sq2/x2(1).^2 + Sx2sq2/x2(2).^2 - 2*
S2x1x2/(x2(1)*x2(2)));

%SIGMAbsq: matrix of covariance of the observations b.
%If the observations are independent then SIGMAbsq will be diagonal
only.
%We further assume that all observations have the same variance.
%(a common assumption)
SIGMAbsq1=eye(8)*Shsq1;
SIGMAbsq2=eye(6)*Shsq2;

% %matrix of covariance of the regression parameters
SIGMAxsq1=K1*SIGMAbsq1*K1';
SIGMAxsq2=K2*SIGMAbsq2*K2';

%Suppose we wish to determine the model value at 100 points ranging
from 0 to 4.
%Thus, we now have the vector equation: bm = Am*x
Am1=[ones(1,100);linspace(0.0167,0.2,100)]';
Am2=[ones(1,100);linspace(0.0167,0.2,100)]';

%Finally, we have the matrix of covariance of bm.
%In general, only the diagonal elements of SIGMAbmsq are of interest.
sigmabmsq1=diag(Am1*SIGMAxsq1*Am1');
sigmabmsq2=diag(Am2*SIGMAxsq2*Am2');

%plotting reaction rates with progesterone and corresponding best fit
model
plot(A1(:,2),Y1,'ro',Am1(:,2),Am1*x1, 'r')
hold on

%plotting reaction rates without progesterone and corresponding best
fit model
plot(A2(:,2),Y2,'gx',Am2(:,2),Am2*x2, 'g')
hold on

%plotting the 95% confidence curves
plot(Am1(:,2),Am1*x1+2*sqrt(sigmabmsq1),'r--',Am1(:,2),Am1*x1-
2*sqrt(sigmabmsq1),'r--')
hold on
plot(Am2(:,2),Am2*x2+2*sqrt(sigmabmsq2),'g--',Am2(:,2),Am2*x2-
2*sqrt(sigmabmsq2),'g--')
hold off
box off

```

```

legend('Data1(Reaction rate with progesterone)', 'best-fit model for
Data 1', 'Data2(Reaction rate without progesterone)', ...
'best-fit model for Data 2', '95% confidence line 1 (2\sigma)
interval for Data1', ...
'95% confidence line 2 (2\sigma) interval for Data1', '95%
confidence line 1 (2\sigma) interval for Data2', ...
'95% confidence line 2 (2\sigma) interval for Data2')
xlim([0 0.22])
xlabel('1/S (per mM)')
ylabel('1/R (nmol per (cells min))')

```

### **Calculations for interval:**

We get, for data with progesterone,

$K_m = 11.4122$  mM,  $R_{max} = 8.5868$  nmol/(cells\*min),  $S_{R_{max}} = 2.9353$  and  $S_{K_m} = 7.3926$

So, 68% confidence interval, assuming normal distribution,  
for  $K_m = (11.4122 - 7.3926)$  to  $(11.4122 + 7.3926) = 4.0196$  , 18.8048;  
for  $R_{max} = (8.5868 - 2.9353)$  to  $(8.5868 + 2.9353) = 5.6515$  , 11.5221

And for data with progesterone,

$K_m = 10.5428$  mM,  $R_{max} = 7.4242$  8.5868 nmol/(cells\*min),  $S_{R_{max}} = 1.0902$  and  $S_{K_m} = 2.8862$

So, 68% confidence interval, assuming normal distribution,  
for  $K_m = (10.5428 - 2.8862)$  to  $(10.5428 + 2.8862) = 7.6566$  , 13.429;  
for  $R_{max} = (7.4242 - 1.0902)$  to  $(7.4242 + 1.0902) = 6.334$  , 8.5144.

### **Comment:**

Since the 95% confidence intervals overlap here for both kinds of data, we can say that Michaelis constants, with and without progesterone treatment, are not significantly different.

## Plots:

