Solution Sheet 02

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```
library(Iso)
```

```
## Iso 0.0-18.1
```

```
load("E:/TUD/04.Semester/toxicology-I/assignments/2/Simulated-Isotonic.RData")
conc <-  c(rep(0, 4), rep(1, 3), rep(2, 5), rep(3, 6), rep(4, 4), rep(5, 5))
```
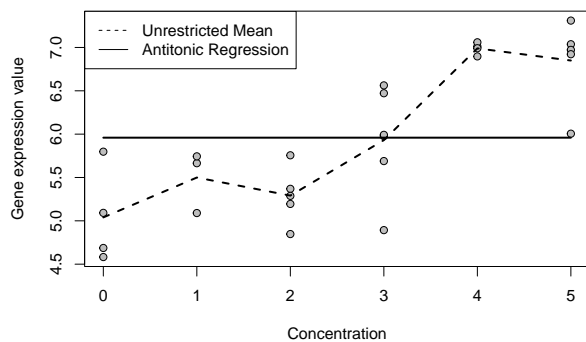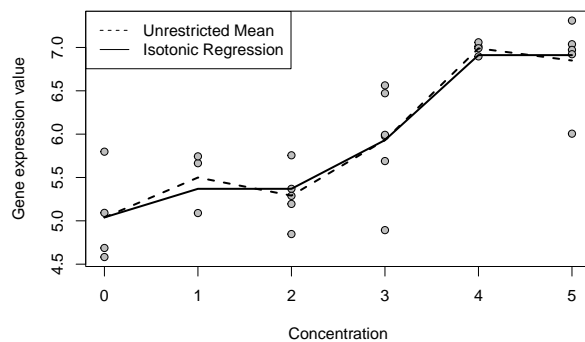
Gene 1

```
plot(
  conc,
  Simulated.Isotonic[, "ExprGene1"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  unique(conc),
  tapply(Simulated.Isotonic[, "ExprGene1"], conc, mean),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  unique(conc),
  pava(tapply(Simulated.Isotonic[, "ExprGene1"], conc, mean), c(4, 3, 5, 6, 4, 5)),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topleft",
  legend = c("Unrestricted Mean", "Isotonic Regression"),
  lty = c(2, 1)
)
plot(
```

```
  conc,
  Simulated.Isotonic[, "ExprGene1"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  unique(conc),
  tapply(Simulated.Isotonic[, "ExprGene1"], conc, mean),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  unique(conc),
  pava(
    tapply(Simulated.Isotonic[, "ExprGene1"], conc, mean),
    c(4, 3, 5, 6, 4, 5),
    decreasing = TRUE
  ),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topleft",
  legend = c("Unrestricted Mean", "Antitonic Regression"),
  lty = c(2, 1)
)
```


Gene 2

```
plot(
  conc,
  Simulated.Isotonic[, "ExprGene2"],
```
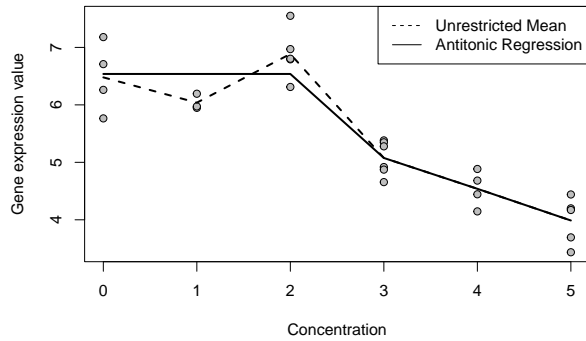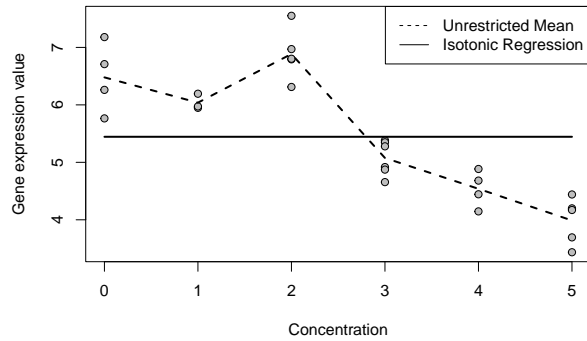
```
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  unique(conc),
  tapply(Simulated.Isotonic[, "ExprGene2"], conc, mean),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  unique(conc),
  pava(tapply(Simulated.Isotonic[, "ExprGene2"], conc, mean), c(4, 3, 5, 6, 4, 5)),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topright",
  legend = c("Unrestricted Mean", "Isotonic Regression"),
  lty = c(2, 1)
)
plot(
  conc,
  Simulated.Isotonic[, "ExprGene2"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  unique(conc),
  tapply(Simulated.Isotonic[, "ExprGene2"], conc, mean),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  unique(conc),
  pava(
    tapply(Simulated.Isotonic[, "ExprGene2"], conc, mean),
    c(4, 3, 5, 6, 4, 5),
    decreasing = TRUE
  ),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topright",
  legend = c("Unrestricted Mean", "Antitonic Regression"),
```
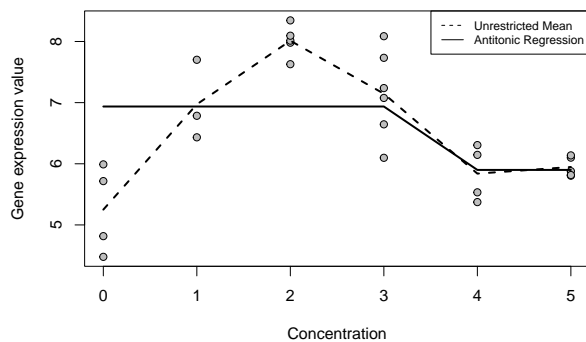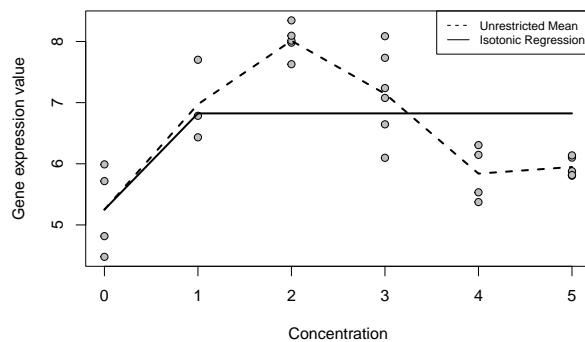
```
  lty = c(2, 1)
)
```


Gene 3

```
plot(
  conc,
  Simulated.Isotonic[, "ExprGene3"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  unique(conc),
  tapply(Simulated.Isotonic[, "ExprGene3"], conc, mean),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  unique(conc),
  pava(tapply(Simulated.Isotonic[, "ExprGene3"], conc, mean), c(4, 3, 5, 6, 4, 5)),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topright",
  legend = c("Unrestricted Mean", "Isotonic Regression"),
  lty = c(2, 1),
  cex = 0.75
)
plot(
  conc,
  Simulated.Isotonic[, "ExprGene3"],
```

```
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  unique(conc),
  tapply(Simulated.Isotonic[, "ExprGene3"], conc, mean),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  unique(conc),
  pava(
    tapply(Simulated.Isotonic[, "ExprGene3"], conc, mean),
    c(4, 3, 5, 6, 4, 5),
    decreasing = TRUE
  ),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topright",
  legend = c("Unrestricted Mean", "Antitonic Regression"),
  lty = c(2, 1),
  cex = 0.75
)
```


Reverse of each genes
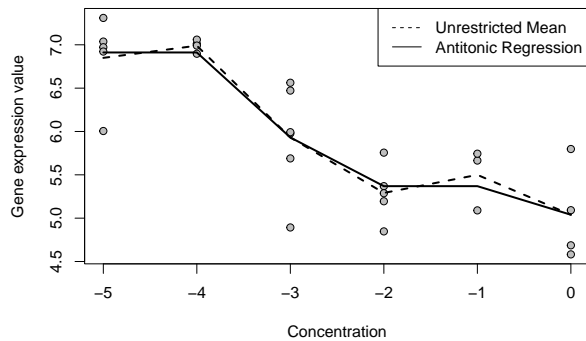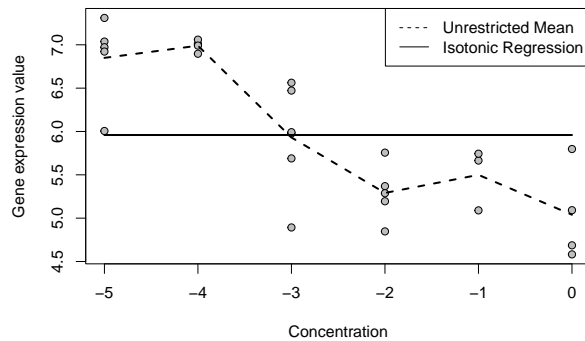
Gene 1

```
plot(
  -conc,
```

```
  Simulated.Isotonic[, "ExprGene1"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  rev(-unique(conc)),
  rev(tapply(Simulated.Isotonic[, "ExprGene1"], conc, mean)),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  rev(-unique(conc)),
  pava(rev(tapply(
    Simulated.Isotonic[, "ExprGene1"], conc, mean
  )), rev(c(4, 3, 5, 6, 4, 5))),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topright",
  legend = c("Unrestricted Mean", "Isotonic Regression"),
  lty = c(2, 1)
)
plot(
  -conc,
  Simulated.Isotonic[, "ExprGene1"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  rev(-unique(conc)),
  rev(tapply(Simulated.Isotonic[, "ExprGene1"], conc, mean)),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  rev(-unique(conc)),
  pava(rev(tapply(
    Simulated.Isotonic[, "ExprGene1"], conc, mean
  )), rev(c(4, 3, 5, 6, 4, 5)),
  decreasing = TRUE),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
```

```
  "topright",
  legend = c("Unrestricted Mean", "Antitonic Regression"),
  lty = c(2, 1)
)
```
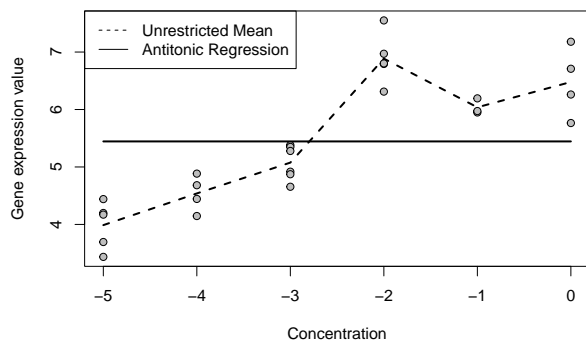

Gene 2

```
plot(
  -conc,
  Simulated.Isotonic[, "ExprGene2"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  rev(-unique(conc)),
  rev(tapply(Simulated.Isotonic[, "ExprGene2"], conc, mean)),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  rev(-unique(conc)),
  pava(rev(tapply(
    Simulated.Isotonic[, "ExprGene2"], conc, mean
  )), rev(c(4, 3, 5, 6, 4, 5))),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topleft",
  legend = c("Unrestricted Mean", "Isotonic Regression"),
  lty = c(2, 1)
)
plot(
```
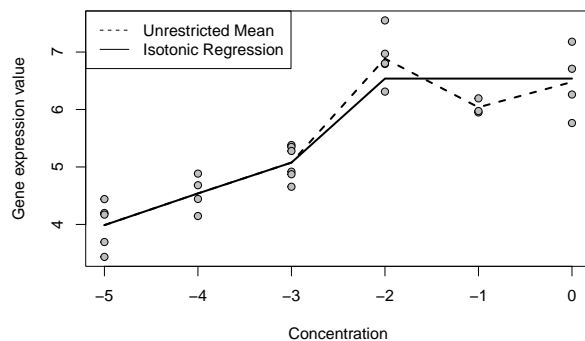
```
  -conc,
  Simulated.Isotonic[, "ExprGene2"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  rev(-unique(conc)),
  rev(tapply(Simulated.Isotonic[, "ExprGene2"], conc, mean)),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  rev(-unique(conc)),
  pava(rev(tapply(
    Simulated.Isotonic[, "ExprGene2"], conc, mean
  )), rev(c(4, 3, 5, 6, 4, 5)),
  decreasing = TRUE),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topleft",
  legend = c("Unrestricted Mean", "Antitonic Regression"),
  lty = c(2, 1)
)
```


Gene 3

```
plot(
  -conc,
  Simulated.Isotonic[, "ExprGene3"],
  pch = 21,
  bg = "grey",
```
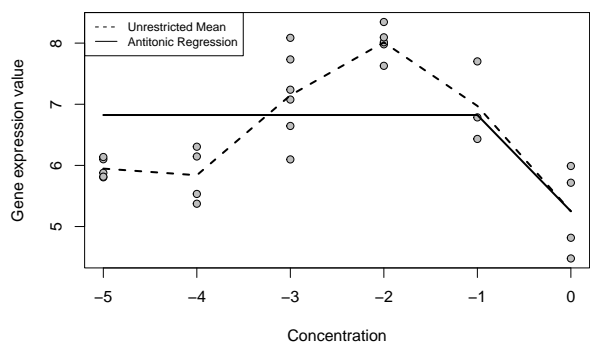
```r
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  rev(-unique(conc)),
  rev(tapply(Simulated.Isotonic[, "ExprGene3"], conc, mean)),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  rev(-unique(conc)),
  pava(rev(tapply(
    Simulated.Isotonic[, "ExprGene3"], conc, mean
  )), rev(c(4, 3, 5, 6, 4, 5))),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topleft",
  legend = c("Unrestricted Mean", "Isotonic Regression"),
  lty = c(2, 1),
  cex = 0.75
)
plot(
  -conc,
  Simulated.Isotonic[, "ExprGene3"],
  pch = 21,
  bg = "grey",
  xlab = "Concentration",
  ylab = "Gene expression value"
)
points(
  rev(-unique(conc)),
  rev(tapply(Simulated.Isotonic[, "ExprGene3"], conc, mean)),
  type = "l",
  lty = 2,
  lwd = 2
)
points(
  rev(-unique(conc)),
  pava(rev(tapply(
    Simulated.Isotonic[, "ExprGene3"], conc, mean
  )), rev(c(4, 3, 5, 6, 4, 5)),
  decreasing = TRUE),
  type = "l",
  lty = 1,
  lwd = 2
)
legend(
  "topleft",
  legend = c("Unrestricted Mean", "Antitonic Regression"),
```
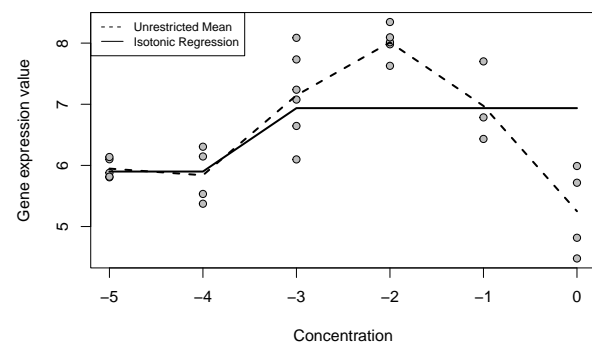
```
  lty = c(2, 1),
  cex = 0.75
)
```

Exercise 02

PAVA - I

c) Perform PAVA on data by hand to obtain Isotonic regression.

Concentrations	x_1	x_2	x_3	x_4	x_5	x_6	x_7
	0.5	2.5	1.5	4.5	2	1.5	5
$\hat{\mu}(x_i)$							
n_i	3	3	7	8	6	4	2

$x_2 < x_3 < x_4 < x_5 < x_6 < x_7$,

$\hat{\mu}(x_i)$ — MLE of responses,

n_i — sample sizes, $i = 1 \ldots 7$

$\Rightarrow$ We got the first violation at $\boxed{i = 2}$.

since, $\hat{\mu}(x_2) = 2.5 > \hat{\mu}(x_3) = 1.5$

$\Rightarrow$ Hence, we pool the observations for 2 conflicting values:

$$\hat{\mu}(x_i, x_{i+1}) = \frac{n_i \hat{\mu}(x_i) + n_{i+1} \hat{\mu}(x_{i+1})}{n_i + n_{i+1}}$$

$$\hat{\mu}(x_2, x_3) = \frac{n_2 \hat{\mu}(x_2) + n_3 \hat{\mu}(x_3)}{n_2 + n_3} = \frac{3 \times 2.5 + 7 \times 1.5}{3 + 7}$$

$$= 1.5$$

$\Rightarrow$ Now, $i = 2, 3$ are pooled

with $\hat{\mu}(x_2, x_3) = \underline{1.5}$.

$\Rightarrow$ At $i = 4$, $\hat{\mu}(x_4) = 4.5$, we got violation,

since $\hat{\mu}(x_4) > \hat{\mu}(x_5) = 2$

Hence, $\hat{\mu}(x_4, x_5) = \frac{n_4 \hat{\mu}(x_4) + n_5 \hat{\mu}(x_5)}{n_4 + n_5} = \frac{8 \times 4.5 + 6 \times 2}{8 + 6} = \frac{48}{14} \approx 3.4286$

$\approx \underline{3.43}$

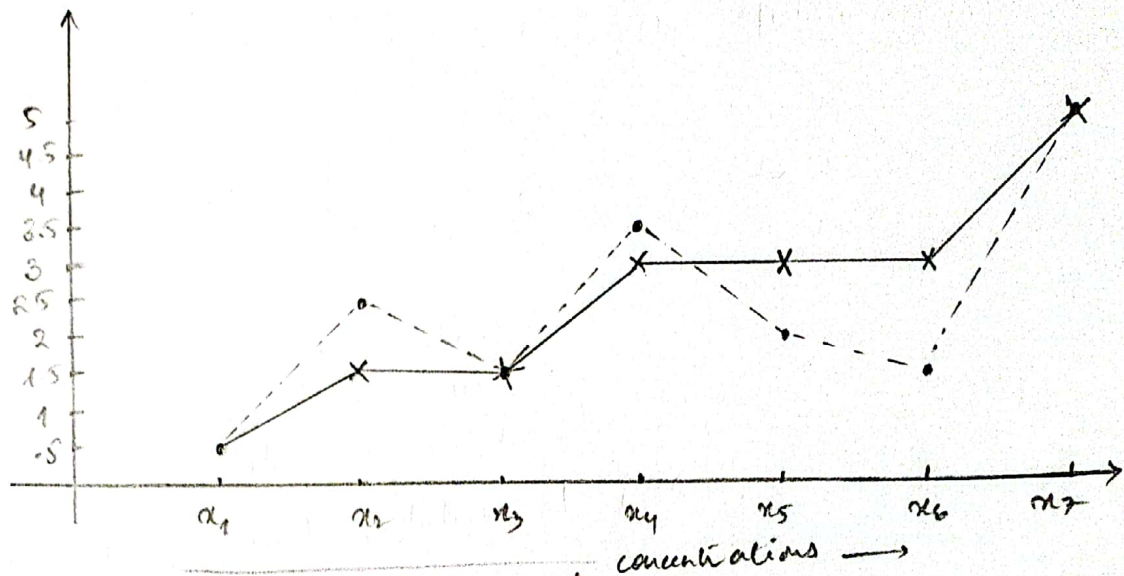$\rightarrow$ At $i = 6$, we got 2nd violation, since $\hat{\mu}(x_4, x_5) > \hat{\mu}(x_6) = 1.5$

we pooled,

$\hat{\mu}(x_4, x_5, x_6) = \frac{n_4 x_4 + n_5 x_5 + n_6 x_6}{n_4 + n_5 + n_6} = \frac{8 \times 4.5 + 6 \times 2 + 4 \times 1.5}{8 + 6 + 4}$

$= \frac{54}{18} \approx 3.00$

$\rightarrow$ At $i = 7$, $\hat{\mu}(x_4, x_5, x_6) < \hat{\mu}(x_7) = 5$

So, no violation further.

we will stop the algorithm.

final result :—

$\boxed{(\, 0.5, \, 1.5, \, 1.5, \, 3.00, 3.00, 3.00, \, 5\,)}$

MLE $\hat{\mu}(\text{mi})$

concentrations →
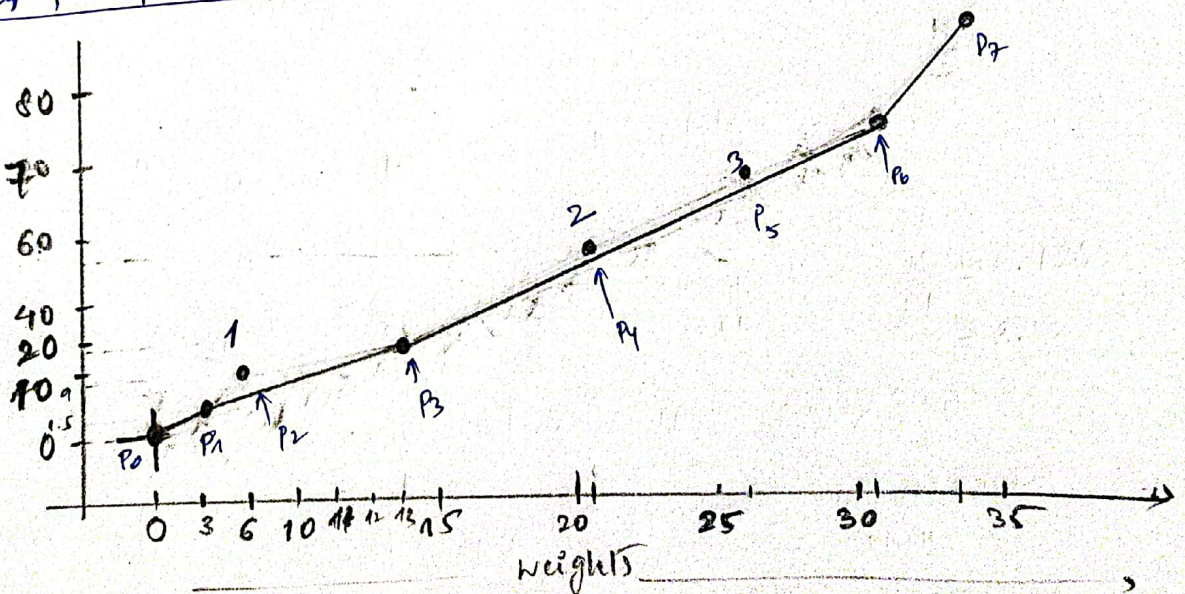
b) Calculate CSD and GCM by hand.

CSD — Cumulative Sum Diagram
GCM — Greatest Convex Minorant.

	W_L	$G_L(x_i)$
x_1	3	1.5
x_2	6	9
x_3	13	19.5
x_4	21	55.5
x_5	27	67.5
x_6	31	73.5
x_7	33	83.5

— GCM
• CSD

weights

The points 1 & 2,3 are above line of plot GCM, which need to plot
in their own segments of line.
GCM has 4 line segments from (P_0 to P_1, P_1 to P_3, P_3 to P_6, P_6 to P_7)
PAVA yields 4 set of results from $P_1 = 0.5$
" $P_2, P_3 = 1.5$ Ans
" $P_4, P_5, P_6 = 3$
" $P_7 = 5$.