4.1 Assume that the counting processes $N_i(t)$; $i = 1, 2, \ldots, n$; have intensity processes of the form $\lambda_i(t) = Y_i(t)\alpha_0(t)\exp(\boldsymbol{\beta}^T \mathbf{x}_i)$, where the $Y_i(t)$ are at risk indicators and the $\mathbf{x}_i = (x_{i1}, \ldots, x_{ip})^T$ are fixed covariates, and let $L(\boldsymbol{\beta})$ be the partial likelihood (4.7) with $r(\boldsymbol{\beta}, \mathbf{x}_i) = \exp(\boldsymbol{\beta}^T \mathbf{x}_i)$.

a) Derive the vector of score functions $\mathbf{U}(\boldsymbol{\beta}) = \log L(\boldsymbol{\beta})/\partial \boldsymbol{\beta}$.
b) Derive the observed information matrix $\mathbf{I}(\boldsymbol{\beta}) = -\mathbf{U}(\boldsymbol{\beta})/\partial \boldsymbol{\beta}^T$.

```
> res.cox = coxph(Surv(futime,death) ~ age + sex + mspike,data=mgus)
> summary(res.cox)
Call:
coxph(formula = Surv(futime, death) ~ age + sex + mspike, data = mgus)

  n= 241, number of events= 225

             coef      exp(coef)  se(coef)      z        Pr(>|z|)
age       0.066748  1.069026  0.007051   9.466   <2e-16 ***
sexmale   0.236694  1.267053  0.136816   1.730   0.0836 .
mspike   -0.084901  0.918603  0.170947  -0.497   0.6194
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

          exp(coef)  exp(-coef)  lower .95  upper .95
age        1.0690     0.9354     1.0544     1.084
sexmale    1.2671     0.7892     0.9690     1.657
mspike     0.9186     1.0886     0.6571     1.284

Concordance= 0.689  (se = 0.019 )
Likelihood ratio test = 104  on 3 df,   p=<2e-16
Wald test            = 96.48  on 3 df,   p=<2e-16
Score (logrank) test = 100.2  on 3 df,   p=<2e-16

> res.cox$var
           [,1]          [,2]          [,3]
[1,]  4.972337e-05 -7.378061e-05 4.857322e-05
[2,] -7.378061e-05  1.871872e-02 1.957005e-04
[3,]  4.857322e-05  1.957005e-04 2.922280e-02
```

3 **Introduction**: The R output below shows some results when estimating a Cox model to a survival data set of 241 individuals with monoclonal gammopathy of undetermined significance (MGUS). The fitted model has three covariates: age, sex and mspike. The covariate sex is binary, whereas the covariates age and mpsike are both continuous. In the data set the values of the covariate age varies from 34 to 90, and the values for mspike varies from 0.3 to 3.2.

Problem: Write down the estimated relative risk function.

Find a 95% confidence interval for the ratio of the hazard rate for a female of age 50 years over the hazard rate of a female of age 51 years, when the mspike value is the same.

Find a 95% confidence interval for the relative risk function for a male of age 35 years and with mspike value equal to 1.5.