School of Biosciences

WRITTEN EXAMINATION

Course: Biomarkers in Molecular Medicine

Sub-course

Course code: BV705A

Credits for written examination 4 hp

Date: 17/1 2025

Examination time: 8:15 – 12:30

Examination responsible: Andreas Tilevik

Teachers concerned

Aid at the exam/appendices: calculator

Write your answers directly in the exam sheets!

No negative points for the multiple-choice questions will be given. You can only get two or zero points on these questions. To get points on these questions, all correct statements must be selected and all incorrect statements must be unselected.

Grade points 40 p.

Examination results should be made public within 18 working days

Good luck!

Describe how biomarkers are currently used in medicine, drug discovery, and environmental health (23 p)

1. Which of the following statements are correct regarding the biomarker discovery process (zero, one or several statements can be correct)? (2p)

   ☐ The identification phase usually involves more subjects (samples) than the validation phase.
   ☐ The identification phase usually involves more variables that are measured (for example more proteins or more genes) than the validation phase.
   ☐ The validation phase should include the same subjects (e.g. people) as the ones that were included in the verification phase.
   ☐ The qualification phase usually involves the same experimental technique as in the identification phase.

2. Name at least two biomarkers that can be used to predict kidney failure and describe the underlying process that causes different levels of these biomarkers in blood and/or urine. (4p)

3. Name one predictive biomarker and explain how it can be used in personalized treatments for cancer. (1 p)

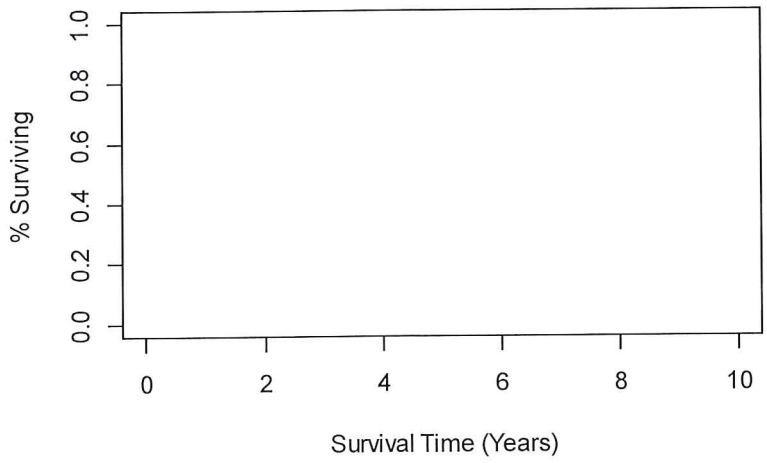
4. Name one diagnostic biomarker and explain what it can be used for. (1 p)

5. Name one biomarker for risk assessments and give an example of a disease that it can be used for. (1 p)

6. Explain what may cause a decrease (1p) or an increase (1p) in the total serum protein level. Your answer should include examples of proteins that may be altered during certain conditions.

7. Draw an approximate survival curve in the plot below based on the data in the following table. (4p)

Patient ID	Survival time (years)	Event (0=censored, 1 = event)
1	2	1
2	6	1
3	6	1
4	10	0
5	10	0



8. Which of the following statements are correct regarding the biomarkers for autoimmune diseases (zero, one or several statements can be correct)? (2p)

☐ CRP is a general marker for inflammation and is sometimes used as a supportive marker for autoimmune diseases.
☐ IgE antibodies are commonly used as a general marker for autoimmune diseases.
☐ The proteins albumin and gp120 are common markers for Rheumatoid arthritis (RA).
☐ Glucose concentration is used as a biomarker to adjust insulin therapy in patients with type 1 diabetes.

9. Which of the following statements are correct regarding the biomarker CRP (zero, one or several statements can be correct)? (2p)

☐ CRP can be detected from a blood sample.
☐ The CRP level is usually lower in patients with viral infections compared to patients with bacterial infections.
☐ CRP can differentiate between all types of autoimmune diseases with high accuracy.
☐ CRP is a general biomarker for detecting inflammatory diseases such as autoimmune diseases and sepsis.

10. Which of the following statements are correct regarding biomarkers for liver diseases (zero, one or several statements can be correct)? (2p)

☐ Bilirubin is a waste product of the breakdown of red blood cells.
☐ A high level of bilirubin in the serum may be used as an indication of reduced liver function.
☐ A low level of albumin in the serum is an indication of reduced liver function.
☐ A high level of unconjugated bilirubin in the serum is an indication of Gilbert's syndrome.

11. Which of the following statements are correct regarding biomarkers for pregnancy and how a pregnancy test works (zero, one or several statements can be correct)? (2p)

☐ Human chorionic gonadotropin (hCG) is a common biomarker used to confirm pregnancy.
☐ The positive control should result in a positive test result (usually a color) to make sure that the test actually works.
☐ If the positive control results in a positive test result, the test is not reliable.
☐ A person who is pregnant will produce antibodies that will be detected in the pregnancy test.

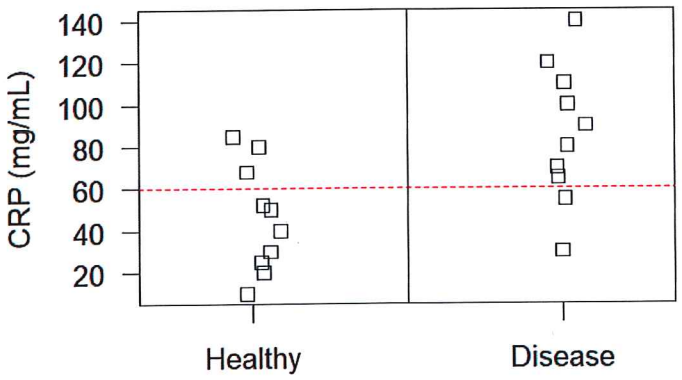
Describe how bioinformatics tools can be used for biomarker discovery (17 p).

1. Imagine that you have measured the concentration of PSA to detect prostate cancer. You have collected the following data: (3p)

Subject	State	PSA concentration (ng/ml)
1	Healthy	1
2	Healthy	2
3	Healthy	3
4	Prostate cancer	3
5	Prostate cancer	4

Show the calculations that you need to do for the first round of iteration when using the Leave-One-Out Cross-validation method. You therefore only need to show the calculations of the cutoff values when the first person is left out and show how this person is predicted based on your cutoff values.

2. In a study, one has evaluated the blood CRP concentration as a biomarker for a certain autoimmune disease. In total, 10 healthy controls and 10 patients with the disease were included in the study. The research group decided to use a cutoff value of 60. Values above this cutoff value are associated with a positive test result, whereas values below this cutoff are associated with a negative test result.



a) How many false negative results are there? (1p)

b) How many true negative results are there? (1p)

c) How many false positive results are there? (1p)

d) Given the cutoff value, what is the sensitivity of the test? **Show your calculations.** (1p)

e) Given the cutoff value, what is the specificity of the test? **Show your calculations.** (1p)

f) Given the cutoff value, what is the negative predictive value? Assume the same prevalence as observed in the sample. **Show your calculations.** (1p)

g) What is the positive likelihood ratio (LR+)? **Show your calculations.** (1p)

h) What is the negative likelihood ratio (LR-)? **Show your calculations.** (1p)

3. Suppose that one has validated a biomarker and calculated the positive likelihood ratio to 4.0. Explain what this value means (show that you can interpret such a value). (2p)

4. Which of the following statements are correct regarding the negative/positive predictive value (NPV/PPV) and accuracy (zero, one or several statements can be correct)? (2p)

☐ The PPV is the probability that you have the disease, given a positive test result.
☐ The accuracy is the sum of the true negatives divided by the sum of all positives and negatives.
☐ The accuracy is the sum of the true positives divided by the sum of all positives and negatives.
☐ The NPV is the probability that you are healthy, given a positive test result.

5. Which of the following statements are correct regarding computational methods that can combine biomarkers (zero, one or several statements can be correct)? (2p)

☐ LDA makes its predictions based on the majority of its five closest neighbors.
☐ The KNN method combines the variables by optimizing its weights.
☐ The KNN method determines the class of the unknown (new) observation based on the majority class of its K closest neighbors of known class.
☐ The KNN method and the LDA method work exactly the same and will result in the same accuracy.