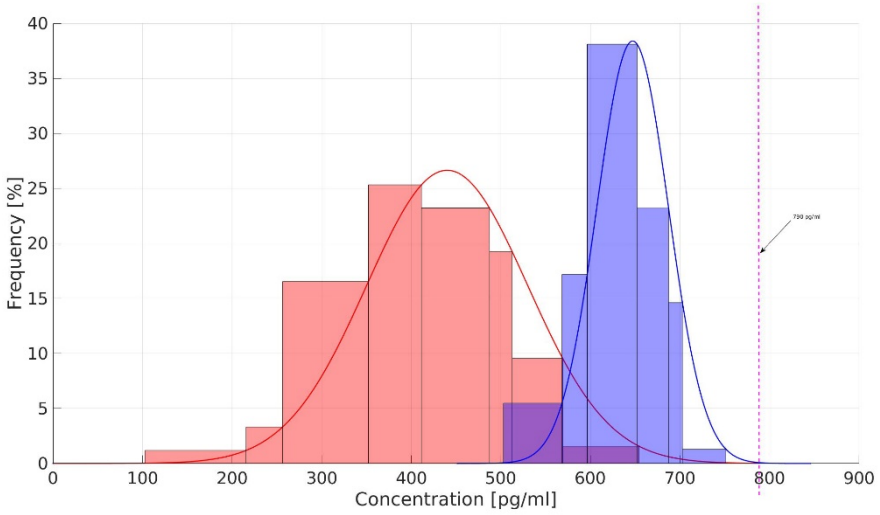
EE515 2024-2025

Fundamentals of Biosensors and Electronic Biochips

SOLUTION SESSION 6: READ, USE AND EVALUATE HOW RELEVANT IS A DIAGNOSTIC BINARY TEST

Exercise 1.

1.a Population distribution:



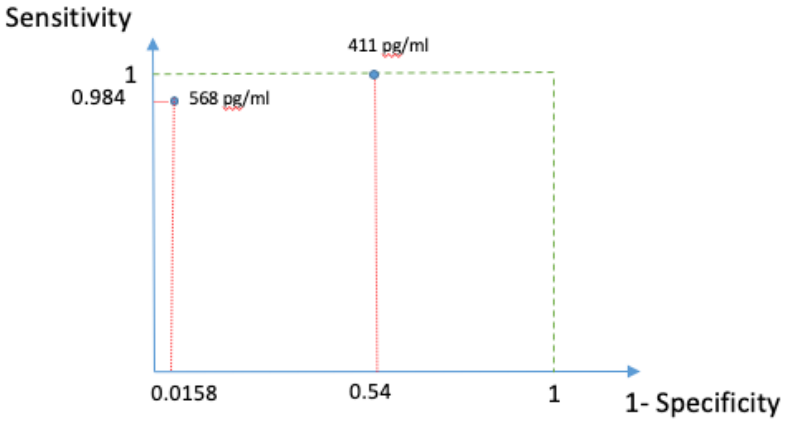
1.b We can read on the graph above that if the specificity is 1 the best sensitivity can be obtained for a concentration of 790 pg/ml.

1.c

Specificity (TH: 411 pg/ml) =

$$\sum_{concentration\ of\ control\ population<411\ pg/ml} frequencies\ for\ control\ population = 46.39\%$$

1.d To draw the ROC curve we need to calculate the sensitivity and specificity for different concentration threshold.



1.e Considering the threshold of 487.27pg/ mL (ASSAY A) we can derive from the data:

Sensitivity $=1$ and Specificity $= 0.696$

Considering the threshold of 568.94 pg/mL (ASSAY B) we can derive:

Sensitivity ≈ 1 and Specificity $= 0.984$

The precision is calculated as following:

$$\text{Precision} = \frac{\text{Prevalence} * \text{Sensitivity}}{\text{Prevalence} * \text{Sensitivity} + (1 - \text{Prevalence})(1 - \text{Specificity})}$$

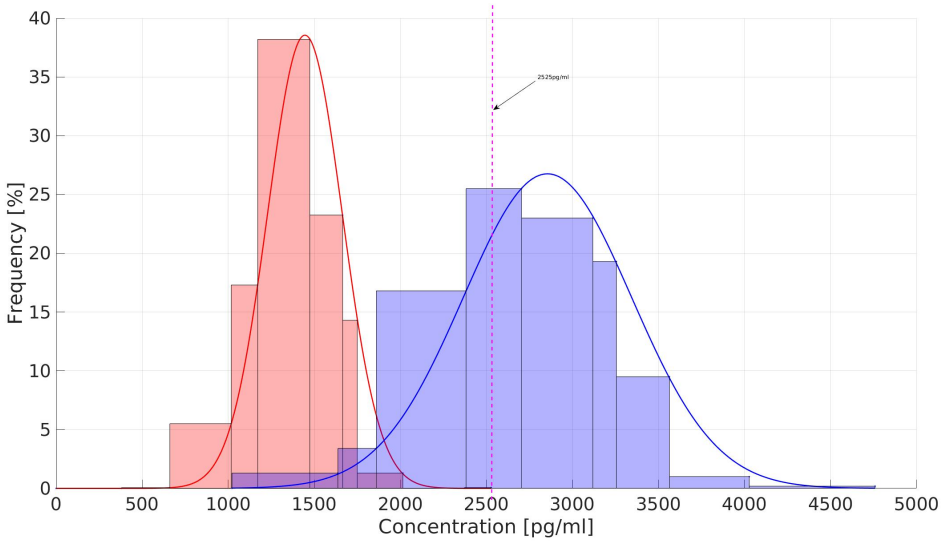
In case of the less specific test (ASSAY A), a prevalence of 1% determines a precision of only 3.5% (probability to have a cancer knowing that you are tested positive), which makes the test irrelevant.

In case of ASSAY B (an almost ideal test, with great specificity and sensitivity), precision is still quite low: 36.7%.

For more critical prevalence of the disease in the population (30%), ASSAY A and ASSAY B grant 58.5% precision and 96.4% precision, respectively. A prevalence of 30% is sufficient to make the ideal assay (ASSAY B) also very precise, while the limited specificity of ASSAY A reflects in a more limited precision (58.5%).

Exercise 2.

2.a Population distribution:



2.b Threshold at around 2528 pg/ml. Start counting true positive from 2705 pg/ml: sensitivity =

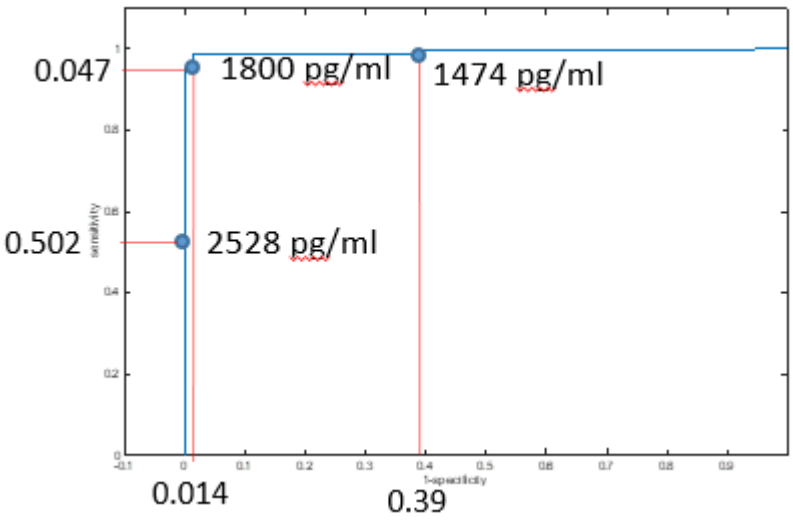
$$\sum_{concentration\ of\ cancer\ population > 2705\ pg/ml} frequencies\ for\ cancer\ population = 52.99\%$$

2.c Specificity (TH: 1800 pg/ml) = Stopping counting true negative from 1750 pg/ml

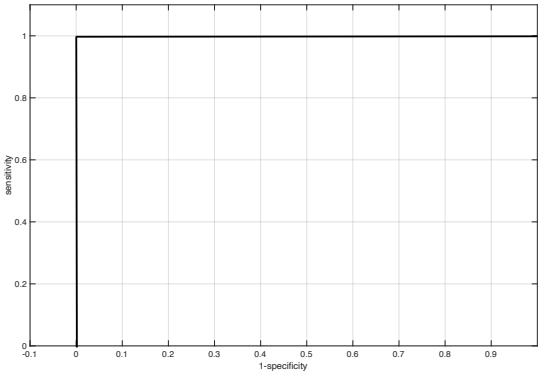
$$\sum_{concentration\ of\ control\ population < 1750 pg/ml} frequencies\ for\ control\ population = 98.6\%$$

It corresponds to the true negative rate.

2.d To draw the ROC curve we need to calculate the sensitivity and specificity for different concentration threshold.



2.e In the ideal case we want no overlap between both curves, which means there will be no false positive and no false negative. If we place our threshold in the no overlapping zone then both sensitivity and specificity will be equal to 1, so the ideal ROC curve will look as the following



Exercise 3.

3.a

1- **Blue** – early stage – area under the curve is smaller, indicating that for a threshold at high specificity we will get smaller sensitivity. This is due to the fact, that in the early stage the biomarker concentration is lower than in later stage. Thus, the population distribution of healthy and disease population will be overlapping (see picture below), and it will be harder to distinguish between them.

   Orange – late stage – area under the curve is larger – almost equal to 1; the population distributions are well distinguishable, there is only small overlap (see picture below), this is characteristic for late stage, where biomarker concentration is higher.

2- The graph is not up to scale, the thresholds are positioned only approximately.

3.b