Deacon's Challenge No. 72 Answer

You receive two blood samples from a general practice, each of which is labelled with the same pre-printed label, but you suspect that they are actually from two different patients. The measured serum sodium concentrations of the two samples are 140 and 143 mmol/L respectively. Given that the high control for your sodium assay runs a standard deviation of 1.07 mmol/L at 151.6 mmol/L and the intra-individual biological variation of serum sodium concentration is quoted as 0.6%, determine whether it is possible that these samples are indeed from the same patient, stating any assumptions that you make.

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We have two results, x_1 and x_2 each of which we will assume belongs to a Gaussian distribution, with respective standard deviation s_1 and s_2. The difference between the two results $(x_1 - x_2)$ will be normally distributed with a combined standard deviation $(s_{1,2})$. If the two samples are from the same patient then the values for the *mean* for each population will be identical so that their difference (*mean* x_1 – *mean* x_2) is zero. Therefore a z value can be calculated to test the null hypothesis that the observed difference between the two results is not significantly different from zero:

$$z = \frac{(x_1 - x_2) - 0}{s_{1,2}}$$

The total standard deviation $(s_{1,2})$ when two results are combined (i.e. added or subtracted) is the square root of the sum of their squares:

$$s_{1,2} = \sqrt{(s_1^2 + s_2^2)}$$

However, if the samples are indeed from the same patient, then $s_1 = s_2$ and this expression simplifies to:

$$s_{1,2} = \sqrt{(s^2 + s^2)} = \sqrt{(2s^2)} = \sqrt{2} \times s = 1.414\,s$$

Therefore the expression for z becomes:

$$\boxed{z = \frac{(x_1 - x_2) - 0}{1.414\,s}}$$

We are given the analytical standard deviation (s) at 151.6 mmol/L but are not told if, or how, this varies with concentration. Therefore it is reasonable to assume that this s value also applies at 143 and 140 mmol/L.

We are not told if there were dates and times on the samples or whether they arrived from the GP practice together or on separate occasions. There are two different scenarios:

1. *The patient was only bled once and two tubes of blood were taken at the same time.* In this instance the intra-individual biological *CV* can be safely ignored since the hypothesis we are testing is that the samples are from the same patient and taken at the same time (in which case the biological variation is zero).

   Substituting 143 mmol/L for x_1 and 140 mmol/L for x_2 and using the analytical standard deviation for sodium (1.07 mmol/L) for s allows evaluation of z:

   $$z = \frac{(143 - 140) - 0}{1.414 \times 1.07} = 1.98$$

   From tables of z the probability of obtaining a z value of 1.96 is 0.05 (or 5%). Since the z value is slightly greater than this we can conclude that **it is unlikely (but not impossible) that both results were from identical samples.**

   An alternative approach to this question is to calculate the maximum difference between the two results which will be significantly different from zero at the 5% level. This can be done by substituting $z = 1.96$ into the above equation followed by re-arrangement:

   $$1.96 = \frac{(x_1 - x_2) - 0}{1.414\,s}$$

   $$(x_1 - x_2) = 1.96 \times 1.414 \times s$$

   $$(x_1 - x_2) = 2.8\,s$$

Therefore if the difference between the two results is less than 2.8 standard deviations then the difference is not significant at the 5% level of probability.

2. *The patient was bled twice so that the samples were taken on separate occasions.* In this case biological variation should be taken into account although if the time interval was very small e.g. the patient was recalled the same day to be bled again because the first sample was temporarily mislaid, then the quoted biological variation may be an over estimate.

First convert the *CV* (%) into standard deviation (s) at the mean concentration (141.5 mmol/L) then estimate the overall standard deviation:

$$s = \frac{CV(\%) \times mean}{100} = \frac{0.6 \times 141.5}{100} = 0.85 \text{ mmol/L}$$

$$s_{Total} = \sqrt{(s_{Analytical}^2 + s_{Intra\text{-}individual}^2)} = \sqrt{(1.07^2 + 0.85^2)}$$

$$= \sqrt{(1.14 + 0.72)} = \sqrt{1.86} = 1.36$$

Recalculation of the z value:

$$z = \frac{(143 - 140) - 0}{1.414 \times 1.36} = \frac{3}{1.92} = \mathbf{1.56}$$

From tables the probability of obtaining a z value of 1.56 is greater than 0.10 so that **it is possible the two samples were from the same patient.**

Question 73

You need to make up a phosphate buffer with a pH of 7.4 and a total phosphate concentration of 50 mmol/L. Calculate the amounts of sodium dihydrogen phosphate and disodium monohydrogen phosphate that need to be weighed into 1 litre of water, given that the pKa is 6.82 (atomic weights: Na 23, P 31).

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