Statistic of suspended blood cells. A new approach

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Summary

A new physical approach to prove the Poisson distribution, based on physical considerations and checked with χ^2-value, is described. Testing various distributions with the proposed physical model in different counters for suspended cells shows clearly that the Poisson distribution is the best fitting distribution, which therefore should replace the binomial distribution [1]. Further one can show with experimental data that, if the normal distribution fits better, there is a substantial amount of random errors. So the proposed method seems to be an easy and simple tool for evaluation of various cell analyzing systems.

Introduction

It is well known that the knowledge of the correct statistics is one of the basics for interpretating quantitative results of manual and machine count. The statistics should be supported and proved by experimental data. The authors never did find any experimental or theoretical justification modelled on experimental data of the commonly used binomial distribution in hematology applications.

Material and methods

100 × 100 white cell differential count under microscope.

To proof cell counting and differential counts done by various machines we tested white cell differential count with different machines.

Results

Experimental data

After selecting proper group intervals for the histograms, we calculated a χ^2-value as an indication of the goodness of fit with three different statistical distributions. Best fit is found in case of manual count with Poisson distribution; only bands and monocytes, which are known to be susceptible to misinterpretation, are best fitted by Gaussian distribution (Table 1).

By checking the fit to the three distributions for two different machines the best fit is found to Poisson distribution or Gaussian distribution gives the best fit (Table 2).

These data suggests that in the case of Gaussian distribution the Poisson distribution is dominated by a random distribution reflecting misinterpretation problems.

Table 1. χ^2-values of manual count (100 x 100 cells)

	Binomial distribution	Poisson distribution	Gaussian distribution
Segmented neutrophils	0.42	0.34	3.30
Band neutrophils	85.00	13.00	4.40
Lymphocytes	0.65	0.17	1.10
Monocytes	60.00	6.60	2.70
Eosinophils	12.00	8.10	11.00
Basophils	105.00	1.70	11.50

Table 2. χ^2-values of automatic count with one of the tested machines

	Binomial distribution	Poisson distribution	Gaussian distribution
Segmented neutrophils	0.78	0.43	1.61
Lymphocytes	1.32	0.98	3.60
Monocytes	0.75	0.37	1.75
Eosinophils	34.90	9.50	2.24
Basophils	0.42	0.57	0.90

Theory

Blood smear

To describe the physical condition we mentally divide the blood smear into different non-overlapping small areas ΔF. If the blood is smeared ideally, then the chance of finding one cell in one area ΔF does not depend on the position of this specific area. In addition there should not be interaction – attraction or repulsion between cells. C_F is the average number of specific cells per area F. We established a system of linear equations, which is taken as an approximate model. The probability of finding n cells of a specific type in an area F is described as $P_n(F)$ with

$$P_n(F) = \frac{(c_F \cdot F)^n}{n!} \cdot \exp(c_F \cdot F)$$

Machine differential count

The physical situation in counters is different from the situation in manual differential count. In order for a counter to register a specific cell, that cell must be preceded by a certain small time interval – called dead time – during which no particle arrives at the counter. It is found [2] that according to this dead time counting losses up to 20 % may occur. Additionally we must take into account the problem that only a simplified recognition algorithm of specific cells is used. This simplified recognition algorithm uses fixed or variable thresholds or cluster analysis procedures and very strongly depends on the causal relationship between the physical signal and the measured non-morphological characteristics of the specific cell, which in some instruments is analog to the cytochemical staining [3] and in other cases is a relationship between protein content of cytoplasma and absorption of high-frequency signals [4].

The Markov characteristic of counting events may be written as

$$P(E(n)/\Delta t) = \frac{dn}{dt} \cdot \Delta t + o(\Delta t)$$

Where $0(\Delta t)$ is the coincidence probability. The solution of the counting process is the Poisson distribution:

$$P(E(n)/\Delta t) = \frac{n^{-n_0}}{n!} \cdot e$$

Discussion

The authors showed with χ^2-values calculated from experimental data that there is strong evidence against using the Binomial but the Poisson distribution as the correct probability model for the counting process. Additionally, it was shown that the Poisson distribution is logically founded. The standard deviation S and the coefficient of variation CV% of the Poisson distribution is easily calculated by:

$$s = \sqrt{n}$$

$$CV\% = \frac{100\ \%}{\sqrt{n}}$$

We have further found that for some cell classes, which are known to be susceptible to misinterpretation, the Gaussian distribution shows the best fit. It is concluded that in cases of correct identification of specific cells the Poisson distribution and in cases of doubtful interpretation the Gaussian distribution is the correct distribution.

Literatur

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