On Contacts of Immunocompetent Cells with Antigen (Note on a Probability Model)

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Abstract. This communication continues with the mathematical formulation and solution of some problems connected with the beginning of the immunological reaction. This paper generalizes some previous results concerning the probability of the event that such a contact of an immunocompetent cell (ICC) with antigen, which is followed by the differentiation of this cell towards the antibody forming cell (AbFC), takes place. Previous papers considered the onset of the differentiation of an ICC caused by the contact of this cell with at least a certain threshold amount of antigen (assuming that these contacts form a non-homogeneous Poisson process). This paper is based on the more general and more realistic assumption that n such contacts are necessary for the stimulation of ICC differentiation (this new assumption has its origin in some new biological findings on the nature of the contact considered, and corresponds with the idea that the differentiation of ICC does not begin until the antigen is bound on a certain fixed number of receptors on the cell surface). Under this assumption, the probability of the event that the differentiation of the cell begins at all (i.e. that at least n contacts will take place), and the probability distribution of the epoch of the beginning of the differentiation (i.e. of the epoch at which the nth contact take place), are derived. — If necessary, these new forms of probability distributions may be used (instead of previous ones) as building stones in models of ICC differentiation.

This paper continues in developing the mathematical theory based on the unitarian concept of an immune reaction (see, e.g., Jílek, 1967).

In previous papers concerning the beginning of differentiation of ICC towards AbFC (Jílek & Ursíniová 1970a, b) it was assumed that for the beginning of the ICC differentiation towards AbFC it was necessary for the antigen to give some unit impulse to the ICC, and that these impulses formed a non-homogeneous Poisson process. The present paper is based on the hypothesis that on the surface of ICC there are a certain (fixed) number of receptors which are available to bind the given antigen (some amount of receptors on the surface of ICC were found in Mitchison's experiments — Mitchison, 1967). It is assumed, for simplicity, that these receptors are identical. For the entering of ICC into the differentiation process it is necessary for the antigen to be bound on at least a certain (fixed) number of these receptors.

This article gives formulae for the probability that at least n contacts will take place, and for the probability density, characteristic function and moments of the epoch*) of the nth contact of an ICC with an antigen. The first part of this paper is devoted to the general case, the second to the particular but important case, in which an exponential decrease in the amount of the injected antigen is considered. (Of course, some other particular cases, not mentioned here, may be solved in a similar way.)

General case

Let us consider a non-homogeneous Poisson process with the intensity function $\lambda(t)$; we assume, for simplicity, that the function $\lambda(t)$ is (at least) piecewise continuous (this assumption will be satisfied in most applications). Then

*) For the term epoch, see Jílek and Ursíniová 1970b.
the probability density of the epoch at which the \( n \)th event occurs (\( n \)th contact of an ICC with antigen takes place), has the form

\[
f_n(t) = e^{-A(t)} \frac{[A(t)]^{n-1}}{I(n)} \alpha(t)
\]

with

\[
A(t) = \int_0^t \alpha(y) \, dy
\]

(cf. Parzen, 1964, § 4.3).

Let \( N(t) \) be the total number of contacts in the time interval \((0, t)\) (where the epoch 0 means the epoch of the immunization).

Then the probability \( P_{n+} \) that one immunization is followed by at least \( n \) contacts of an ICC with antigen (regardless the epoch of any contact),

\[
P_{n+} = \lim_{t \to \infty} \Pr\{N(t) \geq n\},
\]
equals (as can easily be shown)

\[
P_{n+} = \int_0^\infty f_n(t) \, dt = \frac{\gamma(n, A(\infty))}{I(n)}
\]

with

\[
\gamma(n, x) = \int_0^x e^{-y} y^{n-1} \, dy \quad (n > 0).
\]

If \( A(\infty) = \infty \), then \( \gamma(n, A(\infty)) = I(n) \), and \( P_{n+} = 1 \). In the general case, however, where \( A(\infty) = A < \infty \), we have \( P_{n+} < 1 \), and the numerical value of this probability must be established (e.g. by the use of tables edited by Pearson, 1934, or Pagurova, 1963).

**A. Probability of at least \( n \) contacts**

In the particular case (considered in some previous papers as well —see Šterzl & Jilek, 1967; Jilek & Šterzl, 1970; Jilek & Ursinyová, 1970a,b; Jilek, 1971) in which

\[
\alpha(t) = \alpha e^{-\lambda t}, \quad t \geq 0,
\]

where \( \alpha \geq 0 \) has the meaning of a constant proportional to the amount of antigen injected, and \( \lambda > 0 \) is a constant characterizing the rate of elimination of antigen, \( A = \alpha/\lambda \). Therefore, the probability that after one immunization at least \( n \) contacts of a (given) ICC with antigen will take place is, in this case, equal to

\[
P_{n+} = \frac{\gamma(n, \alpha/\lambda)}{I(n)}.
\]

**B. Probability distribution of the epoch of the \( n \)th contact**

In the particular case considered \( A = \alpha/\lambda < \infty \) (if \( \alpha < \infty \)), and hence \( P_{n+} < 1 \); therefore there is a positive probability that \( n \) contacts of the cell with antigen will never take place, and the probability distribution of the epoch of the \( n \)th contact has neither finite mean value nor finite other moments. However, instead of this distribution we may consider the conditional distribution of the epoch of the \( n \)th contact under the condition that at least \( n \) contacts take place at all; the corresponding probability density

\[
f_{n+}(t) = \frac{f_n(t)}{P_{n+}}
\]

has, in the particular case under study, the form

\[
f_{n+}(t) = \frac{\alpha A^{n-1}}{\gamma(n, A)} e^{-\lambda t}(1 - e^{-\lambda t})^{n-1} e^{-A(1-e^{-\lambda t})}, \quad t \geq 0.
\]