A Theory of the Action of X-rays on living Cells. By J. A. Crowther, Sc.D., St John's College.

[*Received* 13 March, *read* 15 March, 1926.]

The absorption by matter of energy from a beam of X-rays follows laws which are now well known. The first stage is the ejection from the absorbing atom of a high speed electron. This electron, in turn, produces pairs of ions from some of the molecules through which it passes until its energy is all spent. The process is essentially a discontinuous one in space, and the proportion of atoms affected at a given time is always exceedingly minute, even with an intense beam of radiation. With a beam of average intensity an individual atom would suffer ionisation, on an average, about once in a million years.

This discontinuous nature of the absorption of X-rays requires to be taken into account in considering the effect of X-rays on living matter. I have already pointed out* that some of the important structures in a living cell are so minute that the probability of their being affected by the radiation in a given short interval of time, say one minute, is quite small. In the particular instance discussed in the paper referred to, this probability amounted to about 0·058 per minute, on the assumption that ionisation in the particle was sufficient to bring about a biological change. If, on the other hand, we assumed that the actual expulsion of a high-speed electron from the particle was necessary to bring about a biological action, the probability would be even smaller. There does not appear to be sufficient evidence to allow of discrimination between these two possibilities. Such discrimination is not necessary for the purpose of the present paper.

Let λ be the probability that a particle of a given kind will be "hit" when unit quantity of X radiation passes through the particles, and let N be the number of such particles present initially. The total number of particles y_0 which are still unaffected by the radiation after a total dose q is given by

$$y_0 = N\epsilon^{-\lambda q}.$$

If a single hit is sufficient to put the particle out of action this equation will give the number surviving a dose q of X radiation. It was suggested in a former paper† that an exponential curve of this kind represented fairly adequately the results of experiments of Strangeways and Oakley‡ on the action of X-rays on tissue cells.

---

* J. A. Crowther, *Proc. Roy. Soc.* B, vol. xcvi, p. 207 (1924).

† *Loc. cit.*

‡ *Proc. Roy. Soc.* B, vol. xcv, p. 373 (1923).

https://doi.org/10.1017/S0305004100009191 Published online by Cambridge University Press

The changes studied by Strangeways and Oakley in these experiments were produced by comparatively small doses of X-rays. Many biological changes require much heavier doses of radiation and the size of particle required for their explanation on the above assumption would be much smaller than we have any evidence for assuming to exist. Moreover, the relation between survival and dosage is certainly not always exponential. More usually, no apparent effect is produced unless the dose exceeds some critical value: the number of survivors then decreases rapidly with increasing dosage, though a few stray specimens survive much larger doses.

A fairly obvious suggestion is that, in such cases, a succession of hits is necessary to produce the effect which is being studied. Many of the cell structures are known to be electrically charged. It may, perhaps, be necessary to neutralise either the whole, or a definite fraction of this charge to produce a change in the structure, just as the neutralisation of the charge on a colloid brings about precipitation. The object of the present paper is to follow out the results of this suggestion.

Since the particles we are considering are large compared with an atom we can assume that the probability of a second, or third hit is the same as that for the first.

Let λ be the probability that a particle of the given kind will be hit once by a quantity of X-rays measured by q, and let y_n be the number which have already been hit n times. The number of these which will be hit again by a small additional dose dq will be $\lambda y_n . dq$. These will pass into the state $(n + 1)$. With the same dose dq, however, a number $\lambda y_{n-1} . dq$ of the particles which have already been hit $n - 1$ times will be hit again and so pass into the state n. Thus we have

$$dy_n = \lambda y_{n-1} . dq - \lambda y_n . dq,$$

$$\frac{dy_n}{dq} = \lambda y_{n-1} - \lambda y_n,$$

$$(D + \lambda)\, y_n = \lambda y_{n-1},$$

writing D for d/dq. Also $y_0 = N\epsilon^{-\lambda q}$. Whence we have

$$y_n = N \frac{\lambda^n q^n}{n!} \epsilon^{-\lambda q}.$$

If n successive hits are required to put the particle out of action, the number surviving a dose q is thus the sum of all the particles in the states for which the number of hits is less than n, i.e.

$$Y = y_0 + y_1 + \dots + y_{n-1}$$

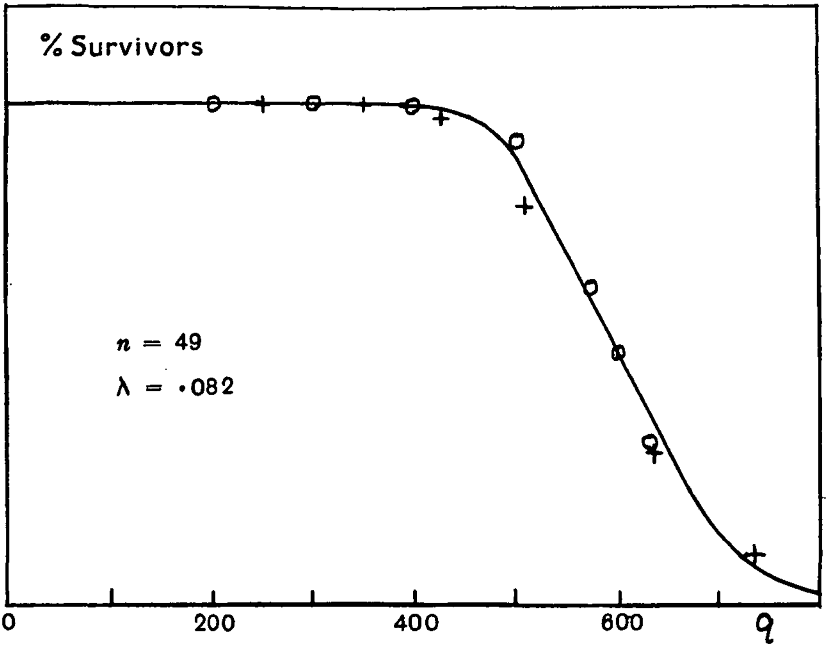
$$= N\epsilon^{-\lambda q}\left(1 + \lambda q + \frac{\lambda^2 q^2}{2!} + \dots + \frac{\lambda^{n-1} q^{n-1}}{\overline{n-1}\,!}\right).$$

https://doi.org/10.1017/S0305004100009191 Published online by Cambridge University Press

The quantity within the bracket consists of the first n terms in the expansion of $\epsilon^{\lambda q}$ and can be put in the form

$$\epsilon^{x}\left(1-\frac{\Gamma_x(n)}{\Gamma(n)}\right),$$

where $x=\lambda q$, $\Gamma(n)$ is the complete gamma function, and $\Gamma_x(n)$ the incomplete gamma function. The ratio $\Gamma_x(n)/\Gamma(n)$ has recently been tabulated by Professor Karl Pearson for an extensive range of values. The computation of the survival curve for given values of n and λ thus presents no difficulties. It is plotted in the accompanying figure, for the values $n=49$, $\lambda=0{\cdot}082$.



A curve of this general shape represents the results of several researches into the action of X-rays on living cells. Unfortunately the numerical results are not sufficiently precise to enable the agreement to be tested numerically. It was thought that suitable material for a test might be found among the protozoa. I have accordingly been making observations on the effect of X-rays on a pure culture of *Colpidium Colpoda*, very kindly supplied to me by Dr Ward Cutler, of Rothamsted. The results of two complete series of such experiments are indicated by the circles and crosses in the figure, the ordinates representing the percentage of individuals surviving a dose of radiation measured by the corresponding

https://doi.org/10.1017/S0305004100009191 Published online by Cambridge University Press

abscissae. The experiments are tedious, and somewhat difficult. The quantity of radiation is measured by ionisation methods, and individual readings of the quantity have a probable error of some 2 or 3 %. Within these limits the two series of experiments agree with each other, and with the theoretical curve with reasonable accuracy. Further experiments are being made with the object of fixing the position of the experimental points with greater precision. Assuming, for the moment, that the theoretical curve drawn is the best fit for the experimental results, they would indicate that Colpidium requires a succession of 49 hits on some particular structure before it is killed by the X radiation. Protozoa are, in fact, highly resistant to the rays, and, as far as I am aware, this is the first time that a lethal effect produced by X-rays has been observed in protozoa of this type.

The experiments have been made possible by a grant from the Government Grant Committee of the Royal Society, to whom I tender my best thanks. I am also deeply indebted to Mr Budden who has very kindly prepared the cultures used in the experiments.

https://doi.org/10.1017/S0305004100009191 Published online by Cambridge University Press