all those quoted by Birks and here, and to account moreover for the relative potencies of the active molecules. It introduces explicitely the requirements for binding which is appropriate for carcinogenesis (binding through the K region) and differentiates it from other types of binding (in particular through the L region) which are not appropriate for carcinogenesis. Moreover, relating carcinogenic activity to chemical and biochemical reactivity, it seems in better direct relation with the protein-deletion hypothesis[8] or with similar theories of a direct interaction of the carcinogen with nucleic acids[9] than are the "physical" theories of the type discussed above, at least in so far as these theories do not suggest any explicit mechanism for the production of tumors. A damage produced in a protein implicated in growth-control or directly in a nucleic acid by a chemical interaction is the simplest hypothesis for the mechanism of action of the chemical carcinogens. Its soundness is to some extent substantiated by the recent results indicating that such may be the mechanism of action of the related mutagens.

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On uncertainties inherent in the determination of the efficiency of collision between virus particles and cells

Several authors (Valentine and Allison[1], Tolmach[2] and Stent and Wollman[3]) have recently concluded, or regarded it as established, that the efficiency of collision of virus particles with cells is near unity. In fact the methods used can only give meaningful values for the collision efficiency if this is less than 10^{-3}–10^{-4}, and are insensitive to higher values. Apart from this limitation, uncertainties in the kinetic theory of liquids prevent the exact measurement of collision efficiency under any conditions.

The literature provides an interesting example of how such a myth can come to be accepted. Valentine and Allison[1] reached their conclusion independently; although their mathematics are correct, they failed to notice that their results are

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quite insensitive to their initial assumption, and therefore do not support it. The interpretation by TOLMACH[2] of his own experiments rests on the same fallacy; he also quotes, in support, STENT AND WOLLMAN[3], PUCK, GAREN AND CLINE[4], DELBRÜCK[5] and SCHLESINGER[6]. Of these, PUCK *et al.* quote DELBRÜCK and SCHLESINGER, basing their conclusion on "extremely high reaction rates". DELBRÜCK uses a correct equation identical with Eqns. 32 and 34 of COLLINS[7], but rightly did not draw any explicit conclusion about the collision efficiency. Nor does SCHLESINGER appear to make any pronouncement on collision efficiency. STENT AND WOLLMAN[3] use a wrong equation, supposed to be derived from the treatment of SMOLUCHOWSKI[8]; this error, which may have been derived from SVESHNIKOFF[9], is noted by COLLINS AND KIMBALL[10] who, with COLLINS[7], have given an exact treatment of the problem. Attention is drawn to the latter authors' work, which will be quoted later; but meanwhile a simple and less precise argument may help to make the point.

Consider the diffusion of particles, of initial concentration c_0 (particles/cm^3), from an infinite medium to a plane surface with which they collide and to which they may adhere. The concentration of particles immediately adjacent to the surface is c'; this is less than c_0 and, provided that it is much less, c' may be taken as constant in expressing the diffusional flux to the surface, and the diffusional flux can be equated to the rate of successful collision. Now the diffusional flux Φ can be expressed in terms of the macroscopic diffusion coefficient D

$$\Phi = (c_0 - c')\sqrt{\frac{D}{\pi t}} \tag{1}$$

Alternatively, D may be replaced by the microscopic expression $\overline{\delta^2}\nu/2$, where $\overline{\delta^2}$ is the mean-square unit jump-length of particles measured at right angles to the surface and ν is the jumping frequency. The collision rate r is expressible only in microscopic terms as

$$r = \frac{c'\bar{\delta}\nu}{2} \tag{2}$$

where $\bar{\delta}$ is the mean jump-length. The rates of diffusion and of successful collision, α being the collision-efficiency (the fraction of collisions leading to adhesion to the surface), can now be equated, necessarily in terms of microscopic quantities:

$$(c_0 - c')\sqrt{\frac{\overline{\delta^2}\nu}{2\pi t}} = \alpha\frac{c'\bar{\delta}\nu}{2} \tag{3}$$

For an ideal gas the ratio $\sqrt{\overline{\delta^2}}/\bar{\delta}$ is $\sqrt{2}$ and we shall not be seriously wrong in taking this value. Eqn. 3 then becomes, with rearrangement

$$\frac{c_0}{c'} - 1 = \alpha\frac{\sqrt{\pi t\nu}}{2} \tag{4}$$

Now the value of Φ (Eqn. 1), which is the rate of adsorption of particles on the surface, does not depend to a measurable degree on c' when c_0/c' is greater than, say, 100. The time of measurement will not normally be less than 100 sec. A rough estimate of ν may be obtained from Eqn. 109 of GLASSTONE, LAIDLER AND EYRING[11] (assuming that $F^*/F = 1$) as 10^{10} sec^{-1}. Inserting these values into Eqn. 4, it is seen that the value of α has no appreciable effect on the measured rate provided that

$\alpha > 10^{-4}$ for $t = 10^2$ sec or $\alpha > 10^{-5}$ for $t = 10^4$ sec. In other words, an experiment of this type cannot do more than demonstrate that the collision efficiency is not less than 10^{-4}–10^{-5}.

The same conclusion can be drawn from the more exact treatment of COLLINS[7]. For the plane case his Eqn. 18 can be written

$$\Phi = c_0\sqrt{\frac{D}{\pi t}}\left\{1 - \frac{\rho^2}{2D\alpha^2 t} + \cdots\right\} \tag{5}$$

where $\rho = \overline{\delta^2}/\bar{\delta}$. If D is taken as $10^{-6}\,\mathrm{cm^2 \cdot sec^{-1}}$ (VALENTINE AND ALLISON[1]), and $\nu = 10^{10}$, then $\overline{\delta^2} = 2 \cdot 10^{-18}$ and $\rho = 2 \cdot 10^{-9}$. For $t = 10^2$, the second term in the bracket is less than 10^{-2} if $\alpha > \sqrt{2} \cdot 10^{-5}$. For adsorption on a spherical surface of radius R, COLLINS (his Eqn. 34) obtains

$$\Phi = 4\pi D c_0 R \cdot \frac{\alpha R}{\alpha R + \rho} \tag{6}$$

For $R = 5 \cdot 10^{-4}$ cm (cells in tissue culture) or $R = 5 \cdot 10^{-5}$ cm (bacteria) the fraction in Eqn. 6 differs from unity by less than 1 % (and Φ is sensibly independent of α) if α is greater than $4 \cdot 10^{-4}$ or $4 \cdot 10^{-3}$, respectively.

One must conclude, therefore, that even in the most favourable case of collision with small spherical objects, the collision efficiency can be *measured* only if it is considerably less than 10^{-3}. Even so, the value would be subject to a considerable uncertainty because of our present lack of exact knowledge of such microscopic quantities as the jump-length and the jump-frequency.

Since submission of this paper it has come to the author's notice that KOCH[12] has already stated clearly the main conclusions of this note.

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