INERT GAS DIFFUSION IN HETEROGENEOUS TISSUE I: WITHOUT PERFUSION

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A mathematical model is proposed to describe transient gas diffusion into a block of heterogeneous tissue placed on an impermeable base. The corresponding asymptotic solution of mass uptake of the gas is derived on the assumption that the diffusion constant is very much smaller in the cellular phase. It is expected that this will be useful in evaluating the diffusion constant in cellular material, and the volume fraction of extracellular fluid, providing the partition coefficient is known.

The phenomenon of mutual interaction and multiple feedback between cellular and extracellular fluid is clearly seen in the overall response of the tissue.

In this regard it is shown that the extraction of the two least dominant time constants, by backward projection of the experimental data curve of gas uptake, is likely to confuse the numerical evaluation of the physical parameters of the system. In an appendix, the problem of diffusion straight through a tissue slice is solved at the asymptotic stage, before steady state is reached. The resulting expression predicts the by-passing of cells by the diffusing gas and shows how the parameters cannot reliably be determined.

Introduction. There is reason to believe that skeletal rabbit muscle behaves as a heterogeneous diffusion medium in the uptake of inert non-polar gases (Hills, 1967). In demonstrating this phenomenon, a thin tissue slice is trimmed to the size of a microscope slide and inserted into a dilatometer. The quantity of acetylene absorbed by the sample is then measured over a period of hours. Since this gas is about 70 times more soluble in aqueous fluids than nitrogen, the volume of gas absorbed is large, resulting in more accurate readings.
The curve of mass $M(t)$ versus time $(t)$ is broken down into the sum of three well separated exponential components by "backward projection."

If the tissue behaves as a homogeneous diffusion medium, then the solution of the linear gas diffusion equation predicts an exponential series (Crank, 1956),

$$M(t) = \sum_{i=0}^{\infty} a_i \exp(-k_i t),$$

of which the first three non-zero components are dominant. The time-constants are of the form

$$k_i = (2i - 1)^2 \pi^2 D^2 / 4l^2, \quad (i = 1, 2, 3, \ldots),$$

where $D$ is the diffusion constant, and $l$ the thickness of the tissue slice.

Thus for a given $l$, the first three time constants extracted should be in the ratio of $1:9:25$. Also, using tissue samples of widely varying $l$, one would expect the law $k\omega l^2$ to be verified.

However no such relationships are observed in actual experiments (Hills, 1967).

The conclusion appears to be that in fact skeletal muscle is a heterogeneous diffusion medium where cellular structure presents a significant barrier to gas uptake.

Before proposing a suitable model which can be subjected to analysis, it is perhaps wise to consider other possible reasons for the variation in the time-constants extracted by backward projection.

In the dilatometer, a small mercury pellet is inserted into the capillary, and its position records the gas uptake into the sample. It is found that both mercury and capillary must be scrupulously clean in order to obtain smooth curves. At the asymptotic stage of the experiment when the rate of mass uptake is slow, such small drag effects on the pellet may in fact indicate a larger final time constant $k_1$ (or smaller half time). Another factor is the diffusion from the sample of water vapour, oxygen, nitrogen and carbon dioxide. These quantities may be very small, but again at the asymptotic stage, the rate of movement of the pellet will decay faster, thus indicating a larger $k_1$ than it actually is.

A more serious factor may be attributed to diffusion into the edges of the tissue slice. Typical dimensions in the worst case are $7.5 \times 2.5 \times 0.3$ cm. The surface area of the edges constitutes $32\%$ of one $7.5 \times 2.5$ face, which is assumed to be the only diffusion surface in the experiment.

Naturally the contribution from the sides will not be very important in extracting the final time constant $k_1$. However extraction of the two earlier constants is almost meaningless, since gas uptake is influenced by edge effects at small to medium times.