THE RAPID AND AUTOMATED CALCULATION OF DIFFUSION COEFFICIENTS IN THIN FILMS, GELS AND TISSUES

S.Hibberd *, J. Adler, M.S. Cheema. Depts. of Theoretical Mechanics*, and Pharmaceutical Sciences, University of Nottingham, Nottingham, NG7 2RD. UK.

The quantitation of drug diffusion in delivery systems and within tissues is of increasing importance. Such studies have been undertaken at a macroscopic level. This work enables quantification of diffusion within microscopic structures such as rate controlling films in controlled delivery devices or cell masses in tissues.
A method for determining diffusion coefficient (D) is described. The methods is similar to that used by Cheema (1985), but can be use to monitor diffusion in structures of dimensions in the order of magnitude of 10^{-6}m. In conjunction with image analysis, diffusion coefficients can be determined within a short time, and without concern for source concentration or boundary effects.
An experimental cell containing gel with zero initial concentration of drug is depicted below:

Fig.1 Schematic diagram of diffusion cell

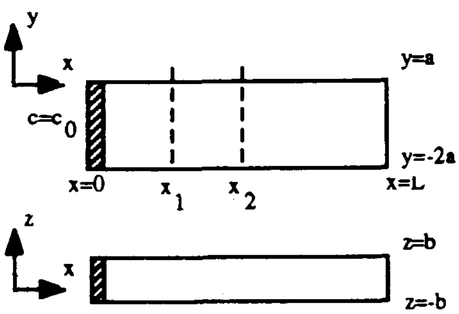

Fig.2 Concentration/time profiles at x_1 and x_2

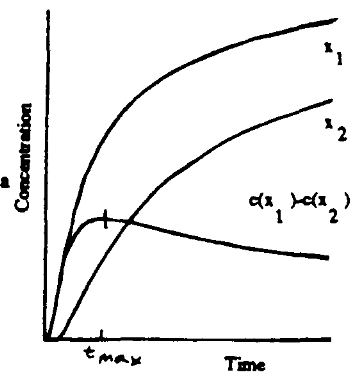

Table1. Diffusion coefficients of fluorescein in crosslinked polyacrylamide gels.

Starting monomer % w/v	t_{max} s	Diffusion coeff. cm^2s^{-1}
10	128	2.731×10^{-6}
15	130	2.689×10^{-6}
20	136	2.570×10^{-6}

Assuming:
i) Length l is sufficient that end effects at x=l are negligible with respect to concentrations measured at x_1 and x_2.
ii) Width 2a is sufficiently wide to negate edge effects where concentrations are measured.
iii) Concentration is uniform throughout the depth 2b.

The diffusion process is monitored at two planes within the gel, at x_1 and x_2., and the difference in diffusant concentration in these two planes recorded as in Fig. 2.. Using microscopic imaging, the dimensions of the measured field can be kept extremely small. This allows monitoring of the diffusion over extremely small distances and hence over short periods.

The difference plot exhibits a maximum at time t_{max} and an equation relating this parameter to D has been derived:

$$D = \left\{ \frac{x_2^2 - x_1^2}{4 \ln (x_2/x_1)} \right\} \frac{1}{t_{max}}$$

This mathematical treatment has been used successfully in conjunction with image analysis and fluorescence microscopy to determine D in a variety of gel forming systems and is being applied to living tissue. With careful selection of x_1 and x_2, it has been possible to determine D for a depth of diffusion of 10×10^{-6} m. and for t_{max} times of less than 30 s.

Cheema, M.S. , Ph.D Thesis, Brighton Polytechnic, 1985.