ACTA STEREOL 1993; 12/2: 85-88
PROC 6ECS PRAGUE, 1993
ORIGINAL SCIENTIFIC PAPER

MEASURING MEMBRANE THICKNESS

Rodney COLEMAN

Department of Mathematics, Imperial College,
180 Queen's Gate, London SW7 2BZ, England

ABSTRACT

An unbiased estimate of the membrane thickness distribution function is given for membranes which are modelled as planar sheets having random thicknesses when they are sampled by isotropic uniform random (IUR) plane sections. The estimate has a simple expression in terms of the intercept measurements. It simplifies the formula given in Mecke (1989).

Key words: sheet thickness distribution, planar probes, stereological unfolding.

INTRODUCTION

The thickness of the air-blood barrier in the lung is related to the lung's function (Weibel and Knight, 1964). The thickness of glomerular basement membrane is affected by diabetes and its treatment (Gundersen and Østerby, 1973). If a micrograph is prepared of a plane section through membrane tissue, measurements made on it of membrane thickness show an apparent thickness rather than the true three-dimensional thickness (Gundersen et al., 1978). Cruz-Orive (1979) models the membranes as isotropic uniform random (IUR) planar sheets. That is to say, the membranes have parallel planar surfaces and a central plane which is IUR relative to the section. In Mecke (1989) membranes are modelled as planar sheets having random thicknesses from a distribution $G(t) = P(T \le t)$. These are sampled by IUR plane sections, and the intercepts with the membranes appear as strips in the sampling planes. The widths of the strips can be measured, and represented by random variables from a distribution $F(\ell) = P(L \le \ell)$. Mecke found an unbiased estimator of the form $u(1/L, 1/t)$ for $G(t)$.

In this note Mecke's solution is expressed more simply. The result is given in the following inversion formula.

INVERSION FORMULA

If the intercept strip has width L, where L has a probability density $f(\ell) = (d/d\ell)F(\ell)$, then

$$G(t) = \int_{\ell=0}^{\infty} h\left(\frac{\ell}{t}\right) f(\ell)\, d\ell = \mathrm{E}h\left(\frac{L}{t}\right), \qquad (1)$$

where E is the symbol for expectation and

$$h(z) = \begin{cases} \frac{1}{2}\left(\frac{1}{\sqrt{1-z^2}} + \sqrt{1-z^2}\right) & (0 < z < 1), \\ 0 & \text{(otherwise)}. \end{cases} \tag{2}$$

AN IUR PLANE INTERSECTING A FIXED PLANE

Let the fixed plane be the horizontal plane, and the random plane have polar coordinates $(x,\omega) = (x,\theta,\phi)$ with respect to an origin of coordinates O in the fixed plane, where x is its distance from O, θ is the latitude, ϕ is the longitude, and ω is a point on the surface of a sphere of unit radius. The random plane is normal to a ray from O through ω. An IUR plane has ω uniformly at random on the surface of the sphere. By symmetry ω can be taken with $0 \le \theta < \pi/2$ and $0 \le \phi < \pi/2$. Then $d\omega = \cos\theta \, d\theta \, d\phi$, and the element of density for the coordinates (x,θ,ϕ) of the IUR plane is $\cos\theta \, dx \, d\theta \, d\phi$.

The line of intersection of the IUR plane with the fixed plane will have polar coordinates (y,ϕ) in the fixed plane with respect to the origin O and axis $\phi = 0$. The transformation to coordinates $y = x \sec\theta$, $\theta = \theta$, $\phi = \phi$ gives the element of density $\cos^2\theta \, dy \, d\theta \, d\phi$ for the coordinates (y,θ,ϕ) ($\cos\theta \, dx \, d\theta \, d\phi = \cos^2\theta \, dy \, d\theta \, d\phi$). This factorizes to give a constant factor for the density for (y,ϕ), demonstrating that the line of intersection is IUR in the fixed plane, and the factor $\cos^2\theta$ for θ . This latter normalizes to give the probability density

$$p(\theta) = \frac{4}{\pi} \cos^2\theta \qquad \left(0 \le \theta < \frac{\pi}{2}\right). \tag{3}$$

This result is well known and can be found in Mecke (1989) and elsewhere.

THE INVERSE PROBLEM

The intercept L satisfies the relationship, $T = L \cos\Theta$, where Θ is the random angle that the normal to the IUR section makes with the surface of the membrane (Fig. 2). The true thickness T is independent of Θ. By symmetry Θ

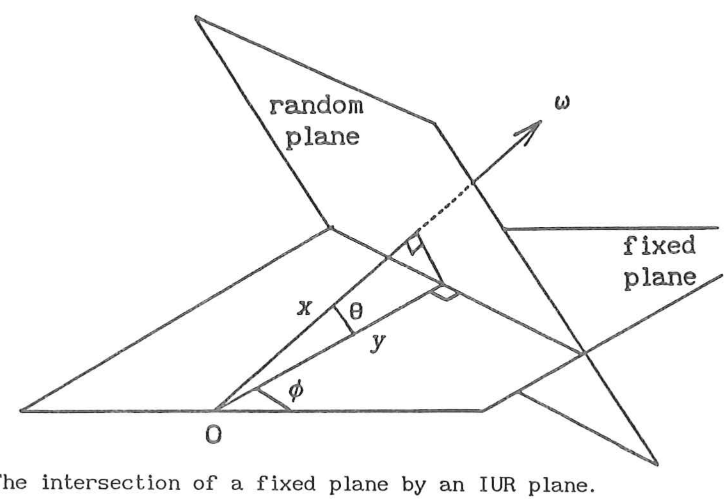

Fig. 1. The intersection of a fixed plane by an IUR plane.

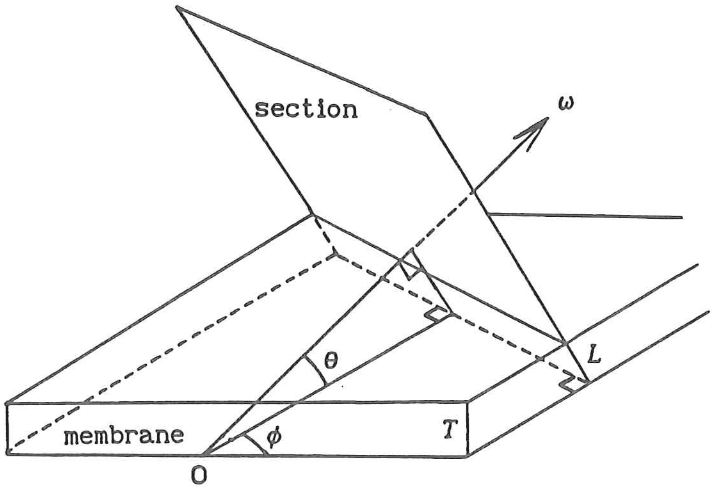

Fig. 2. A planar sheet membrane cut by a plane section.

can be taken to be in the range $0 \le \Theta < \pi/2$. Then

$$P(L \le \ell) = P(T \sec\Theta \le \ell) = \int_{\theta=0}^{\frac{\pi}{2}} P(T \le \ell \cos\theta)\, p(\theta)\, d\theta$$

i.e.

$$F(\ell) = \int_{\theta=0}^{\frac{\pi}{2}} G(\ell \cos\theta)\, \frac{4}{\pi} \cos^2\theta\, d\theta\,. \tag{4}$$

The transformation $t = \ell \cos\theta$ in the integral in (4) gives

$$F(\ell) = \frac{4}{\pi} \int_{t=0}^{\ell} G(t)\, \frac{t^2}{\ell^2} \frac{1}{\sqrt{\ell^2 - t^2}}\, dt\,. \tag{5}$$

The solution (1) can be checked by substituting the formula for G(t) given in (1) into (5).

ESTIMATION

If ℓ_1, ℓ_2, ..., ℓ_n are observations of the widths of the strips of membrane in the IUR sampling plane, then, for any fixed value of t, the average value of $h(\ell_1/t)$, $h(\ell_2/t)$, ..., $h(\ell_n/t)$ is an estimate of G(t). This is equivalent to replacing $f(\ell)$ in (1) by its sample estimator which gives equal weights to each of the observations. The estimate for fixed values of t is unbiased and consistent. However for estimation of the function G(t) over the entire range of t, as t nears the value of an observation, since $h(\ell/t)$ has $\sqrt{(\ell^2-t^2)}$ in its denominator, the estimate tends to infinity before dropping back to zero. The estimate of the probability G(t) is thus not restricted to the range [0,1], and, as t increases, the estimate of the distribution function is not monotone increasing, and so the estimate cannot itself be a distribution function. Further, the ill-conditioning that is known to arise in inverse problems involving Abel type integrals, such as (5) and those arising in the

Wicksell problem, can be expected here also. Methods of regularization which smooth the data or the fitted distribution should be used. See Coleman (1989) for a review of these methods. In conclusion care must be exercised in using the unbiased estimator obtained in this paper.

REFERENCES

Coleman R. Inverse problems. J Microsc 1989; 153: 233-248.

Cruz-Orive LM. Estimation of sheet thickness distributions from linear and plane sections. Biom J 1979; 21: 717-730.

Gundersen HJG, Jensen TB, Østerby R. Distribution of membrane thickness determined by lineal analysis. J Microsc 1978; 113: 27-43.

Gundersen HJG, Østerby R. Statistical analysis of transformations leading to normal distribution of measurements of the peripheral glomerular basement membrane. J Microsc 1973; 97: 293-299.

Mecke J. Mathematical aspects of the stereological membrane problem. In: Hübler A, Nagel W, Ripley BD, Werner G, eds. Geobild '89. Mathematical Research Volume 51. Berlin: Akademie-Verlag, 1989: 117-122.

Weibel ER, Knight BW. A morphometric study on the thickness of the pulmonary air-blood barrier. J Cell Biol 1964; 21: 367-384.

APPENDIX

Various forms for the inversion of equations like (5) may be found. If

$$\phi(\ell) = \int_{t=0}^{\ell} \psi(t) \frac{t^k}{\ell^k} \frac{1}{\sqrt{\ell^2 - t^2}} \, \mathrm{d}t = \int_{t=0}^{\infty} \psi(t)\, h_{kk}\left(\frac{t}{\ell}\right) \frac{1}{\ell} \, \mathrm{d}t \,,$$

where

$$h_{kk}(z) = \begin{cases} z^k (1 - z^2)^{-1/2} & (0 < z < 1)\,, \\ 0 & (\text{otherwise})\,. \end{cases}$$

then it has the solution

$$\psi(t) = \int_{w=0}^{\infty} \phi'(w)\, h_k\left(\frac{w}{t}\right) \mathrm{d}w \,,$$

where

$$h_k(z) = \begin{cases} \dfrac{2}{\pi} \displaystyle\int_{u=0}^{z} \frac{u^{k+1}}{(1 - u^2)^{3/2}} \, \mathrm{d}u & (0 < z < 1)\,, \\ 0 & (\text{otherwise})\,. \end{cases}$$

provided $\phi'(\ell)$, $h_k(z)$ and the integrals exist. By taking

$$\phi(\ell) = \ell^j F(\ell) \,, \qquad \psi(t) = t^j G(t) \,,$$

and varying j and k, different forms of solution to (5) are obtained, one of which reduces to (1). Another gives the unbiased estimator for the sampling of strips in the plane by IUR line sections.