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Abstract

It was a major breakthrough when design-based stereological methods for *vertical sections* were developed by Adrian Baddeley and coworkers in the 1980's. Most importantly, it was shown how to estimate in a design-based fashion surface area from observations in random vertical sections with uniform position and uniform rotation around the vertical axis. The great practical importance of these developments is due to the fact that some biostructures can only be recognized on vertical sections. Later, local design-based estimation of mean particle volume from vertical sections was developed. In the present paper, we review these important advances in stereology. Quite recently, vertical sections have gained renewed interest, since it has been shown that mean particle shape can be estimated from such sections. These new developments are also reviewed in the present paper.

Keywords: marked point processes; stereology; surface area; tensors

1 Introduction

The main practical purpose of stereology is to estimate quantitative parameters of a spatial structure from microscopy images of sections through the structure. A transition from 'classical' to 'modern' stereology occurred in the late 1970's. Modern stereology has rigorous statistical foundations, involving a number of key concepts from survey sampling theory, offering new stereological identities and using a wider range of stochastic models. Design-based as well as model-based methods are available (Baddeley & Jensen, 2005).

Vertical sections play an important role in modern stereology. The initiator of design-based methods for vertical sections is Baddeley (1983, 1984, 1985, 1987) who has had a major impact on the way microscopy images are analyzed, see the highly cited paper Baddeley, Gundersen & Cruz-Orive (1986).

An early and celebrated example of the importance of vertical sectioning was presented by Dr. E. Hasselager at one of the first *Workshops on Stochastic Geometry, Stereology and Image Analysis*. (These workshops are still running every second year. Another important workshop series was the GEOBILD workshops in the former

DDR.) Hasselager wanted to make inference on microvilli in pig placenta, finger-like objects that must be sectioned longitudinally for correct identification, see Hasselager (1986).

Examples of quantitative parameters that can be estimated from vertical sections are volume (Baddeley & Jensen, 2005, p. 179), surface area (Baddeley, 1983, 1984, 1985, 1987; Baddeley, Gundersen & Cruz-Orive, 1986), particle number (Miles, 1978; Sterio, 1984) and mean particle volume (Gundersen, 1988; Jensen & Gundersen, 1993). Recently, it has been shown that also mean particle shape can be estimated from vertical sections (Kousholt et al., 2017; Larsen et al., 2019). Here, volume tensors of rank 0, 1 and 2 are used, from which ellipsoidal approximations to the particles can be constructed.

In the present paper, we review these important advances in stereology. The main focus is on the recent research on estimation of mean particle shape from vertical sections.

The paper is organized as follows. In Section 2, vertical sections are defined, and stereological estimators of volume and surface area from vertical sections are derived. The remaining part of the paper deals with stereological inference for particle populations. The particles are modelled by a stationary marked point process in Section 3, and estimators of particle number and mean particle volume, based on observations in vertical sections, are presented. The estimator of mean particle volume is valid in this model-based setting under the *restricted isotropy assumption*, meaning that the particle distribution is invariant under rotations around the vertical axis. Under the same assumption, an estimator of mean particle shape from vertical sections is described in Section 4. The mean particle shape is represented by the so-called Miles ellipsoid[1] which is a function of mean particle volume tensors of rank 0, 1 and 2. These tensors can be estimated consistently (in a probabilistic sense) from observations in vertical sections.

2 Volume and surface area from vertical sections

A 'vertical' section is a plane L in $\mathbb{R}^3$, which is parallel to a pre-chosen fixed direction, called the 'vertical' direction. Equivalently, a vertical section is a plane, perpendicular to a fixed plane, called the 'horizontal' plane. The vertical direction may be chosen as a special direction in the structure under study, an example is longitudinal sections of muscle tissue. Alternatively, the vertical direction may be chosen for experimental convenience. Some structures can only be recognized on vertical sections.

If we choose a coordinate system in $\mathbb{R}^3$ such that the z-axis is the vertical direction and the xy-plane is the horizontal plane, then a vertical plane is any plane of the following form

$$L = L_{\theta,u} = \{(x, y, z) : x \cos\theta + y \sin\theta = u\},$$

$\theta \in [0, \pi)$ and $u \in \mathbb{R}$. The parameters (θ, u) specify the position of the intersection line between L and the xy-plane. Clearly, the vertical plane is uniquely determined

[1]Roger E. Miles was a pioneer in the development of stereological methods for particle populations with arbitrarily shaped particles.

by its intersection line, see also Figure 1. A natural uniform measure on vertical planes is

$$\mathrm{d}L = \mathrm{d}u\,\mathrm{d}\theta.$$

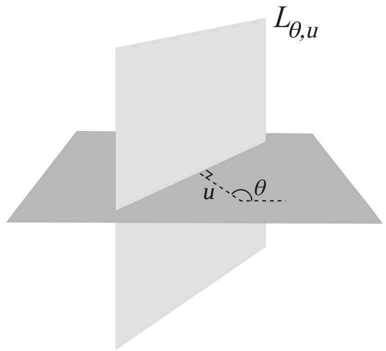

Figure 1: A vertical plane can be parametrized by polar coordinates $\theta \in [0, \pi)$ and $u \in \mathbb{R}$.

Let Y be a compact subset of $\mathbb{R}^3$. It is straightforward to see that the volume (Lebesgue measure) $V(Y)$ of Y can be determined from the areas $A(Y \cap L)$ on vertical planes L. Using the product structure of Lebesgue measure in $\mathbb{R}^3$, we thus have

$$\int_{\text{vertical planes}} A(Y \cap L)\,\mathrm{d}L = \int_0^\pi \int_{-\infty}^{\infty} A(Y \cap L_{\theta,u})\,\mathrm{d}u\,\mathrm{d}\theta = \pi V(Y).$$

The situation is more complicated for quantitative parameters like surface area. Until the beginning of the 1980's, it was actually not possible in a design-based setting to estimate stereologically surface area from observations in vertical sections of the structure under study. The classical stereological methods were based on probes (lines, planes) that had the freedom to be arbitrarily oriented. As an example, the surface area $S(Y)$ of Y, satisfying mild smoothness conditions, was estimated from observation of intersection points on lines T_3 in $\mathbb{R}^3$ that could have any direction in $\mathbb{R}^3$. The basic geometric identity used was the following

$$\int_{\text{lines in } \mathbb{R}^3} N(\partial Y \cap T_3)\,\mathrm{d}T_3 = \pi S(Y),$$

where $N(\partial Y \cap T_3)$ is the number of intersection points between the boundary ∂Y of Y and T_3. If we parametrize the line T_3 in $\mathbb{R}^3$ by (ω, t), where ω is its direction represented as a point on the unit hemi-sphere in $\mathbb{R}^3$ and t is the intersection point between T_3 and the plane $\omega^\perp$ through o perpendicular to ω, then

$$\mathrm{d}T_3 = \mathrm{d}t\,\mathrm{d}\omega,$$

where $\mathrm{d}\omega$ is the element of the uniform measure on the unit hemi-sphere and $\mathrm{d}t$ is the element of two-dimensional Lebesgue measure on $\omega^\perp$.

It was a major breakthrough when Adrian Baddeley developed design-based stereological methods for vertical sections in the 1980's (Baddeley, 1983, 1984, 1985, 1987) and published together with collaborators the highly cited paper Baddeley, Gundersen & Cruz-Orive (1986) in *Journal of Microscopy.* A basic observation was that any non-vertical line in $\mathbb{R}^3$ is contained in a unique vertical plane. The mathematical problem in the case of surface area estimation was therefore to find a decomposition of the measure $\mathrm{d}T_3$ via vertical planes. Such a measure decomposition was already found in Baddeley (1983, p. 13–16), using the coarea formula,

$$\mathrm{d}T_3 = \sin\alpha(T_2)\mathrm{d}T_2\,\mathrm{d}L. \tag{2.1}$$

Here, $\mathrm{d}T_2$ is the element of the uniform measure on lines in L and $\alpha(T_2)$ is the angle between T_2 and the vertical axis. Using (2.1), we find

$$\begin{aligned}\pi S(Y) &= \int_{\text{lines in } \mathbb{R}^3} N(\partial Y \cap T_3)\,\mathrm{d}T_3 \\ &= \int_{\text{vertical planes}} \int_{\text{lines} \subset L} N(\partial Y \cap T_2)\sin\alpha(T_2)\,\mathrm{d}T_2\,\mathrm{d}L \\ &= \int_{\text{vertical planes}} W(\partial Y \cap L)\,\mathrm{d}L, \end{aligned} \tag{2.2}$$

where

$$W(\partial Y \cap L) = \int_{\text{lines} \subset L} N(\partial Y \cap T_2)\sin\alpha(T_2)\,\mathrm{d}T_2. \tag{2.3}$$

Based on (2.2) and (2.3), a number of designs, involving systematic sampling, have been developed for estimating surface area from vertical sections, see Baddeley, Gundersen & Cruz-Orive (1986) or Baddeley & Jensen (2005, 182–187).

Methods as described above have much earlier been derived in a model-based setting by Spektor (1960) and Hilliard (1967) under the assumption that the structure under study is stationary and isotropic with respect to rotations around the vertical axis. The design-based version, derived by Adrian Baddeley, applies to arbitrary orientation distribution of the structure which, of course, is a great advantage.

3 Stereological inference for particle populations

Vertical sections also play an important role in stereological inference for particle populations. We will here treat the model-based case which, we believe, is most appealing for statisticians. For design-based inference on particle populations, see e.g. Baddeley & Jensen (2005, p. 255–269).

3.1 The particle model

We assume that the particles can be modelled by a marked point process

$$\Psi = \{[y_i; Z_i]\},$$

where the ith particle $Y_i = y_i + Z_i$ is represented by a reference point $y_i \in \mathbb{R}^3$ and a mark $Z_i \subset \mathbb{R}^3$. We suppose that the marks are compact subsets of $\mathbb{R}^3$ and the process of reference points $\{y_i\}$ is a point process in $\mathbb{R}^3$, i.e. a locally finite random set in $\mathbb{R}^3$. For an introduction to marked point processes, see e.g. Chiu et al. (2013, Section 4.2).

An important example is the case where the particles are biological cells and the reference points are cell nuclei or some identifiable part of the nuclei such as the nucleoli.

We assume that the marked point process Ψ is stationary, such that

$$\Psi + y = \{[y_i + y; Z_i]\}$$

has the same distribution as Ψ for all $y \in \mathbb{R}^3$. The process of reference points $\{y_i\}$ is thereby also stationary. Its intensity is denoted λ.

Under stationarity, we can give a precise meaning to the particle mark distribution via the so-called intensity measure of the marked point process, also in cases where the marks are not necessarily independent and identically distributed. If we let $\mathcal{C}^3$ be the set of compact subsets of $\mathbb{R}^3$, the intensity measure of Ψ is for measurable sets $A \subseteq \mathbb{R}^3$ and $C \subseteq \mathcal{C}^3$ given by

$$\Lambda_m(A \times C) = \mathbb{E} \sum_i \mathbf{1}\{y_i \in A, Z_i \in C\}.$$

Since Ψ is stationary, $\Lambda_m(\cdot \times C)$ is a translation invariant measure on $\mathbb{R}^3$ and therefore proportional to volume measure $V(\,\cdot\,)$. Accordingly, Λ_m can be decomposed as

$$\Lambda_m(A \times C) = \lambda_C V(A), \tag{3.1}$$

where λ_C is the mean number of particles per unit volume with marks in C. The particle mark distribution is then defined by

$$P_m(C) = \lambda_C / \lambda. \tag{3.2}$$

Combining (3.1) and (3.2), we have

$$\Lambda_m(A \times C) = \lambda V(A) P_m(C). \tag{3.3}$$

We let $\mathbf{Z}_0$ be a random compact set, distributed according to the particle mark distribution P_m. The random set $\mathbf{Z}_0$ may be regarded as a randomly chosen particle or a typical particle with the origin o as its reference point.

3.2 Particle number and mean particle volume from vertical sections

As is common in optical microscopy, we will here study the particle process via sections. An important methodological problem is *sampling bias*. Restricting attention to those particles hit by a plane section introduces a bias: larger particles are more likely to be sampled since they are more likely to be hit by the section plane. The sampling bias is eliminated if we instead sample those particles with reference point in a 3D sampling box W,

$$\mathcal{S} = \{i : y_i \in W\}, \tag{3.4}$$

cf. Figure 2. If $N(\mathcal{S})$ is the number of sampled particles, we clearly have

$$\mathbb{E}\, N(\mathcal{S}) = \mathbb{E} \sum_i \mathbf{1}\{y_i \in W\} = \lambda V(W),$$

so $\hat{\lambda} = N(\mathcal{S})/V(W)$ is an unbiased estimator of λ.

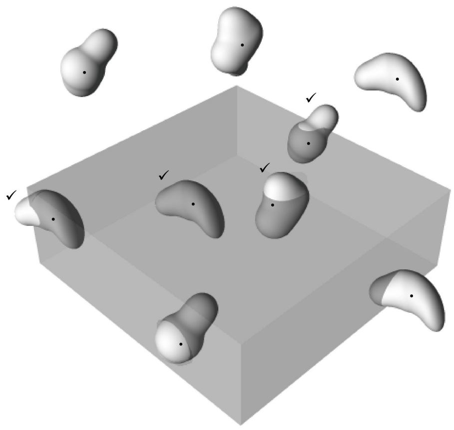

Figure 2: Sampling of particles, using a 3D version of Miles' associated point rule. A particle is sampled if its reference point belongs to the 3D sampling box. Sampled particles are marked by ticks. Reproduced from Baddeley & Jensen (2005) by kind permission of Chapman & Hall/CRC. © 2005 Chapman & Hall/CRC.

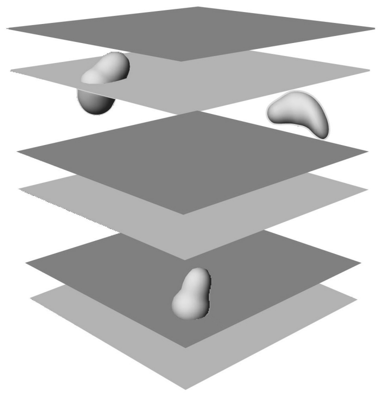

Figure 3: The particles are sampled if they first appear in the space bounded by neighbouring light grey and dark grey planes. If the planes are ordered from top to bottom, only the uppermost particle is sampled by this procedure. Reproduced from Baddeley & Jensen (2005) by kind permission of Chapman & Hall/CRC. © 2005 Chapman & Hall/CRC.

This type of sampling can be performed in optical microscopy where W is generated by moving the focal plane down through a transparent histological slab. The height of W is equal to the distance, travelled by the focal plane. See also the illustration Ziegel, Nyengaard & Jensen (2015, Fig. 4). The sampling procedure is a 3D version of Miles' (Miles, 1974) *associated point rule.* An alternative is to sample those particles with upper-most point in W, cf. Figure 3. This type of sampling design, called the *disector* (Sterio, 1984), has had widespread applications in the biosciences.

Based on the sample of particles (3.4), we can also estimate a mean value $\mathbb{E}\,\varphi(\mathbf{Z}_0)$ in the particle mark distribution where $\varphi(Z)$ is a particle characteristic, such as volume, centre of mass or shape of Z. It follows from (3.3) that

$$\mathbb{E}\sum_{i\in\mathcal{S}}\varphi(Y_i-y_i)=\mathbb{E}\sum_{y_i\in W}\varphi(Z_i)=\lambda V(W)\mathbb{E}\,\varphi(\mathbf{Z}_0),$$

so

$$\frac{\mathbb{E}\sum_{i\in\mathcal{S}}\varphi(Y_i-y_i)}{\mathbb{E}N(\mathcal{S})}=\mathbb{E}\,\varphi(\mathbf{Z}_0),$$

and

$$\sum_{i\in\mathcal{S}}\varphi(Y_i-y_i)/N(\mathcal{S}) \tag{3.5}$$

becomes a ratio-unbiased estimator of $\mathbb{E}\,\varphi(\mathbf{Z}_0)$. Note that each sampled particle Y_i enters into the estimator with its own reference point y_i as origin. If the particle process is ergodic, (3.5) is also a consistent estimator of $\mathbb{E}\,\varphi(\mathbf{Z}_0)$ in an expanding window regime, see Daley & Vere-Jones (2008, Corollary 12.2.V).

For the determination of the estimator (3.5), it is needed to have direct access to the sampled particles in 3D. If this is not possible, stereological methods may be used to estimate $\varphi(Y_i-y_i)$. We will here focus on the situation from optical microscopy where a transparent histological slab, cut vertically from the biostructure under study, is available. Let us suppose that the slab is parallel to a vertical plane L, say. Without loss of generality, we can assume that L passes through the origin o. The observations are

$$y_i,\; Y_i\cap(y_i+L),\qquad i\in\mathcal{S}. \tag{3.6}$$

Here, y_i+L is the focal plane through the reference point y_i of the sampled particle Y_i. Note that, when placing the histological slab onto the microscope stage for observation, the slab will appear horizontal, as shown in Figure 2. A design of this type is called local (Jensen, 1998).

In our model-based setting, the stereological estimators of $\mathbb{E}\varphi(\mathbf{Z}_0)$ are valid under the *restricted isotropy assumption*, meaning that the distribution of $\mathbf{Z}_0$ is invariant under rotations around the vertical axis.

As an example, let us consider estimation of $\mathbb{E}V(\mathbf{Z}_0)$, using the observations (3.6). (In the next section, we consider more involved cases.) Let us choose a coordinate system such that the vertical axis is the z-axis and the vertical plane L is the xz-plane,

$$L=\{(u,0,z):u,z\in\mathbb{R}\}.$$

Using cylindrical coordinates with respect to the z-axis, we have, see Figure 4,

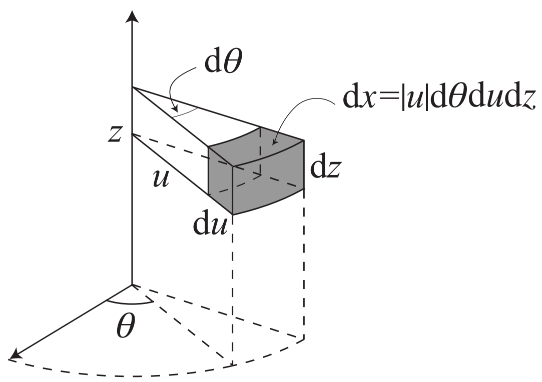

Figure 4: Decomposition of volume measure, using cylindrical coordinates.

$$
\begin{aligned}
\mathbb{E}V(\mathbf{Z}_0) &= \mathbb{E}\int_{\mathbf{Z}_0} \mathrm{d}x \\
&= \int_{z=-\infty}^{\infty}\int_{u=-\infty}^{\infty}\int_{\theta=0}^{\pi} P((u\cos\theta, u\sin\theta, z)\in\mathbf{Z}_0) \\
&\qquad \times |u|\,\mathrm{d}\theta\,\mathrm{d}u\,\mathrm{d}z.
\end{aligned}
$$

Under restricted isotropy, we find

$$
\begin{aligned}
\mathbb{E}V(\mathbf{Z}_0) &= \pi\int_{z=-\infty}^{\infty}\int_{u=-\infty}^{\infty} P((u,0,z)\in\mathbf{Z}_0)|u|\,\mathrm{d}u\,\mathrm{d}z \\
&= \mathbb{E}\widehat{V}(\mathbf{Z}_0\cap L),
\end{aligned}
$$

where

$$
\widehat{V}(Z\cap L) = \pi\int_{Z\cap L} |u|\,\mathrm{d}u\,\mathrm{d}z. \tag{3.7}
$$

It follows that

$$
\sum_{i\in\mathcal{S}} \widehat{V}((Y_i - y_i)\cap L)/N(\mathcal{S}) \tag{3.8}
$$

is a ratio-unbiased estimator of $\mathbb{E}V(\mathbf{Z}_0)$. The estimator (3.8) is also a consistent estimator of $\mathbb{E}V(\mathbf{Z}_0)$ in an expanding window regime if the particle process is ergodic. Note that the estimator (3.8) can be determined from the observations in (3.6), since

$$
(Y_i - y_i)\cap L = [Y_i\cap(y_i + L)] - y_i.
$$

A discretized version of (3.8), called the *vertical rotator*, was presented in Jensen & Gundersen (1993), see also the recent paper Hasselholt et al. (2019).

4 Mean particle volume tensors from vertical sections

Recently, it has been shown under the restricted isotropy assumption that mean particle volume tensors can be estimated from observations in vertical sections (Kousholt et al., 2017). The estimators can be combined to provide a consistent estimator of the Miles ellipsoid. This ellipsoid carries important information about mean particle shape and orientation.

Below, we give a short introduction to volume tensors, present the Miles ellipsoid and its properties, and describe the estimation of mean particle volume tensors from vertical sections. We focus on the model-based setting. A dual design-based approach is discussed in Larsen et al. (2019).

4.1 Volume tensors

For a non-negative integer r, the volume tensor of rank r of a compact subset Y of $\mathbb{R}^3$ is defined by

$$
\Phi_r(Y) = \frac{1}{r!}\int_Y y^r\,\mathrm{d}y. \tag{4.1}
$$

Here, y^r is the symmetric rank r tensor. For $y = (y_1, y_2, y_3) \in \mathbb{R}^3$, y^r can be represented as an array of elements

$$(y^r)_{i_1 i_2 i_3} = y_1^{i_1} y_2^{i_2} y_3^{i_3}, \qquad i_1, i_2, i_3 \in \{0, \ldots, r\}, \sum_{j=1}^{3} i_j = r.$$

The integration in (4.1) is to be understood elementwise.

The volume tensor of rank 0

$$\Phi_0(Y) = \int_Y 1 \, \mathrm{d}y = V(Y)$$

is the volume of Y, while the volume tensor of rank 1 is the following point in $\mathbb{R}^3$

$$\Phi_1(Y) = \left(\int_Y y_1 \, \mathrm{d}y, \int_Y y_2 \, \mathrm{d}y, \int_Y y_3 \, \mathrm{d}y \right).$$

Note that $c(Y) = \Phi_1(Y)/\Phi_0(Y)$ is the centre of mass $c(Y)$ of Y. The volume tensor of rank 2 can be represented as a 3×3 matrix with entries

$$\Phi_2(Y)_{i,j} = \frac{1}{2} \int_Y y_i y_j \, \mathrm{d}y,$$

$i, j = 1, 2, 3$.

Using $\Phi_0(Y)$, $\Phi_1(Y)$ and $\Phi_2(Y)$, we can construct a centred ellipsoid $e(Y)$ of the same volume as Y such that $c(Y) + e(Y)$ is an ellipsoidal approximation to Y, cf. Figure 5. It can be obtained from a spectral decomposition of $\Phi_2(Y - c(Y))$,

$$\Phi_2(Y - c(Y)) = \Phi_2(Y) - \frac{\Phi_1(Y)^2}{2\Phi_0(Y)} = BDB^T,$$

where B is an orthogonal matrix and D is a diagonal matrix with diagonal elements d_i, $i = 1, 2, 3$. The ellipsoid $e(Y)$ has directions of semi-axes equal to the columns of B, lengths of semi-axes proportional to $\sqrt{d_i}$, $i = 1, 2, 3$, and volume equal to $V(Y)$. If Y is an ellipsoid, $Y = c(Y) + e(Y)$, see e.g. Jensen & Ziegel (2014, Section 3).

4.2 The Miles ellipsoid

Let us suppose that the particles can be modelled by a stationary marked point process Ψ, as described in Section 3.1. The Miles ellipsoid $e(\Psi)$ is a centred ellipsoid that provides information about mean particle shape and orientation. The ellipsoid $e(\Psi)$ is determined from $\mathbb{E}\Phi_0(\mathbf{Z}_0)$, $\mathbb{E}\Phi_1(\mathbf{Z}_0)$ and $\mathbb{E}\Phi_2(\mathbf{Z}_0)$, using exactly the same method as the one used for determining $e(Y)$ from $\Phi_0(Y)$, $\Phi_1(Y)$ and $\Phi_2(Y)$. If the particles are translates of the same particle Z_0, then $e(\Psi) = e(Z_0)$, the ellipsoidal approximation to Z_0.

Under the assumption of restricted isotropy, the average orientation of the particles in 3D coincides with the vertical axis. Under restricted isotropy, the Miles ellipsoid $e(\Psi)$ is an ellipsoid of revolution around the vertical axis (Larsen et al., 2019, Appendix A), containing information about mean particle shape. If we let the lenghts of the semi-axes of this Miles ellipsoid $e(\Psi)$, parallel and perpendicular to the vertical axis, be denoted a and b, respectively, then the ratio $I = a/b$ indicates the degree of elongation of the particles in the direction of the vertical axis.

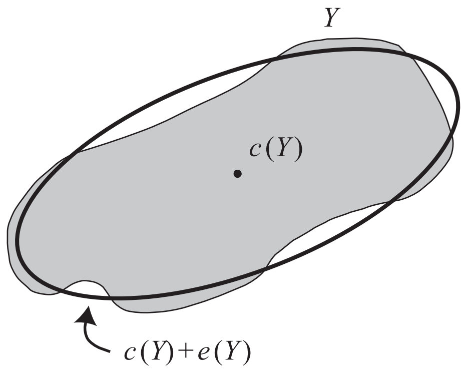

Figure 5: Illustration in 2D of the ellipsoidal approximation to a particle Y. The centre of mass of Y is denoted $c(Y)$, while $e(Y)$ is a centred ellipsoid, such that $c(Y) + e(Y)$ is an ellipsoidal approximation to Y. If Y is an ellipsoid, then $Y = c(Y) + e(Y)$.

4.3 Estimation of mean particle volume tensors

The estimators of mean particle volume tensors can be derived, using the same type of reasoning as the one presented in Section 3 for estimation of $\mathbb{E}V(\mathbf{Z}_0)$. Here, we also choose a coordinate system such that the vertical axis is the z-axis and use cylindrical coordinates with respect to this axis. It turns out to be most convenient to let (θ, u, z) vary in the set $[0, 2\pi) \times \mathbb{R}_+ \times \mathbb{R}$. We get, cf. Kousholt et al. (2017, Section 14.3),

$$\begin{aligned}\mathbb{E}\Phi_r(\mathbf{Z}_0) &= \frac{1}{r!}\mathbb{E}\int_{\mathbf{Z}_0} x^r \,\mathrm{d}x \\ &= \frac{1}{r!}\int_{z=-\infty}^{\infty}\int_{u=0}^{\infty}\int_{\theta=0}^{2\pi} P((u\cos\theta, u\sin\theta, z) \in \mathbf{Z}_0) \\ &\qquad \times (u\cos\theta, u\sin\theta, z)^r u \,\mathrm{d}\theta\,\mathrm{d}u\,\mathrm{d}z \\ &= \int_{z=-\infty}^{\infty}\int_{u=0}^{\infty} P((u,0,z) \in \mathbf{Z}_0) g_r(u,z)\,\mathrm{d}u\,\mathrm{d}z, \end{aligned} \tag{4.2}$$

where we at the third equality sign have used restricted isotropy and $g_r(u, z)$ is the following rank r tensor

$$g_r(u,z) = \frac{1}{r!}\int_{\theta=0}^{2\pi} (u\cos\theta, u\sin\theta, z)^r u\,\mathrm{d}\theta, \qquad u > 0, z \in \mathbb{R}. \tag{4.3}$$

We find

$$\mathbb{E}\Phi_r(\mathbf{Z}_0) = \mathbb{E}\int_{\mathbf{Z}_0 \cap L_+} g_r(u,z)\,\mathrm{d}u\,\mathrm{d}z,$$

where

$$L_+ = \{(u, 0, z) : u > 0, z \in \mathbb{R}\}.$$

Using symmetry arguments, we get

$$\mathbb{E}\Phi_r(\mathbf{Z}_0) = \mathbb{E}\widehat{\Phi}_r(\mathbf{Z}_0 \cap L),$$

where

$$\widehat{\Phi}_r(Z \cap L) = \frac{1}{2}\int_{Z\cap L} g_r(|u|, z)\,\mathrm{d}u\,\mathrm{d}z \tag{4.4}$$

and

$$L = \{(u, 0, z) : u, z \in \mathbb{R}\},$$

as previously. (Note that (4.4) is valid for the actual choice of the z-axis as vertical axis.) The resulting estimators of $\mathbb{E}\Phi_r(\mathbf{Z}_0)$,

$$\sum_{i \in \mathcal{S}} \widehat{\Phi}_r((Y_i - y_i) \cap L)/N(\mathcal{S}), \qquad r \text{ non-negative integer}, \tag{4.5}$$

can be determined from the available observations (3.6). If the particle process is ergodic, the estimators (4.5) are consistent and can for $r = 0, 1, 2$ be combined into a consistent estimator of the Miles ellipsoid $e(\Psi)$.

It follows from Kousholt et al. (2017, p. 427–428) that for $i_1, i_2, i_3 \in \{0, \dots, r\}$ with $\sum_{j=1}^{3} i_j = r$,

$$g_r(u, z)_{i_1 i_2 i_3} = \begin{cases} \frac{1}{r!} c_{i_1 i_2} u^{i_1 + i_2 + 1} z^{i_3}, & i_1, i_2 \text{ even}, \\ 0, & \text{otherwise}, \end{cases}$$

where

$$c_{i_1 i_2} = 2 \frac{\omega_{i_1 + i_2 + 2}}{\omega_{i_1 + i_2 + 1}} \frac{\binom{(i_1 + i_2)/2}{i_1/2}}{\binom{i_1 + i_2}{i_1}}.$$

Here, $\omega_i = 2\pi^{i/2}/\Gamma(i/2)$ is the surface area of the unit sphere in $\mathbb{R}^i$. These results have recently been generalized to $\mathbb{R}^n$ in Eriksen & Kiderlen (2020).

For $r = 0$, we get

$$\widehat{\Phi}_0(Z \cap L) = \pi \int_{Z \cap L} |u| \, \mathrm{d}u \, \mathrm{d}z,$$

as in (3.7), while for $r = 1$ we obtain

$$\widehat{\Phi}_1(Z \cap L) = (0, 0, \pi \int_{Z \cap L} |u| z \, \mathrm{d}u \, \mathrm{d}z).$$

The estimator of $\mathbb{E}\Phi_2(\mathbf{Z}_0)$ can be represented as the following 3×3 matrix

$$\widehat{\Phi}_2(Z \cap L)$$
$$= \begin{pmatrix} \frac{\pi}{4} \int_{Z \cap L} |u|^3 \, \mathrm{d}u \, \mathrm{d}z & 0 & 0 \\ 0 & \frac{\pi}{4} \int_{Z \cap L} |u|^3 \, \mathrm{d}u \, \mathrm{d}z & 0 \\ 0 & 0 & \frac{\pi}{2} \int_{Z \cap L} |u| z^2 \, \mathrm{d}u \, \mathrm{d}z \end{pmatrix}$$

It follows that the resulting estimator of the Miles ellipsoid $e(\Psi)$ is an ellipsoid of revolution around the z-axis, just like $e(\Psi)$.

The non-zero elements of the estimators $\widehat{\Phi}_r(Z \cap L)$ are, apart from known constants, all of the form

$$\int_{Z \cap L} |u|^j z^k \, \mathrm{d}u \, \mathrm{d}z,$$

where j, k are non-negative integers and j is odd. If automatic segmentation of $Z \cap L$ is not available, the integral may be discretized, using e.g. a line grid, perpendicular to the z-axis, see Larsen et al. (2019, p. 11). In this paper, the method has been implemented in human brain tissue, and the precision of the estimators is assessed, using a bootstrap procedure. The method is superiour to an earlier, more time-consuming method (Rafati et al., 2016).

If $\mathbf{Z}_0$ is modelled parametrically, the parameters in the model may be estimated, using the mean particle volume tensors. One example is the Lévy particle model, studied in Kousholt et al. (2017); Rafati et al. (2016); Ziegel, Nyengaard & Jensen (2015), see an illustration in Figure 6.

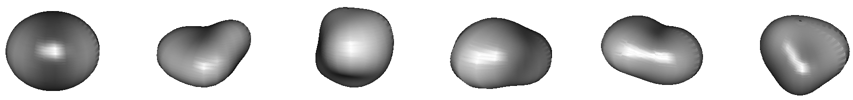

Figure 6: Particles simulated under a Lévy particle model as random deformations of a prolate ellipsoid, shown to the left. Five random deformations are shown. Reproduced from Kousholt et al. (2017) by kind permission of Springer International Publishing. © 2017 Springer International Publishing.

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