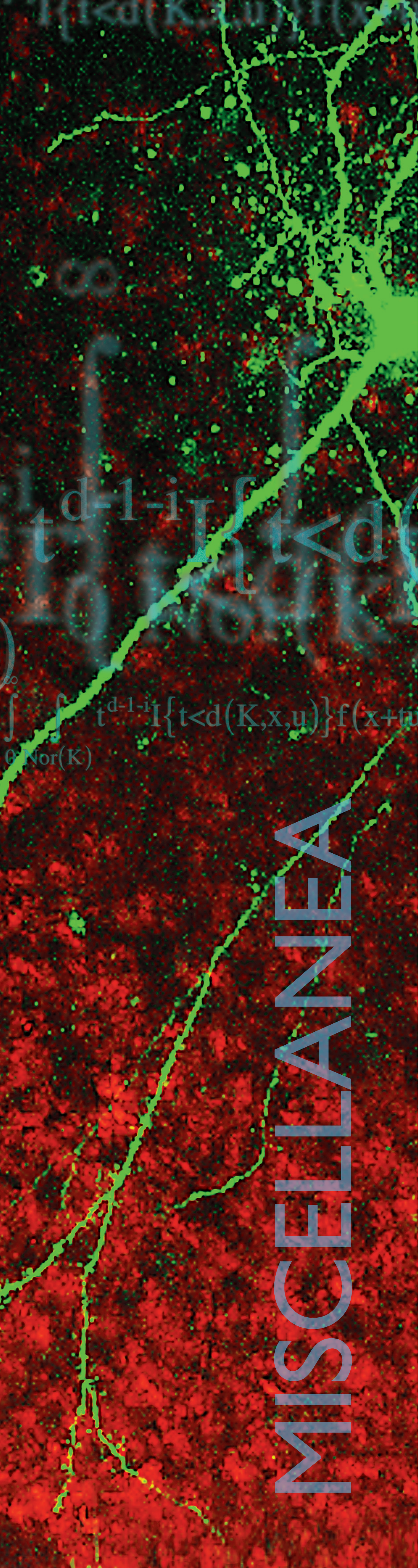

CENTRE FOR **STOCHASTIC GEOMETRY**
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Rotational integral geometry and local stereology – with a view to image analysis

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Rotational integral geometry and local stereology – with a view to image analysis

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Abstract

This chapter contains an introduction to rotational integral geometry that is the key tool in local stereological procedures for estimating quantitative properties of spatial structures. In rotational integral geometry, focus is on integrals of geometric functionals with respect to rotation invariant measures. Rotational integrals of intrinsic volumes are studied. The opposite problem of expressing intrinsic volumes as rotational integrals is also considered. It is shown how to express intrinsic volumes as integrals with respect to geometric functionals defined on lower dimensional linear subspaces. Rotational integral geometry of Minkowski tensors is shortly discussed as well as a principal rotational formula. These tools are then applied in local stereology leading to unbiased stereological estimators of mean intrinsic volumes for isotropic random sets. At the end of the chapter, emphasis is put on how these procedures can be implemented when automatic image analysis is available. Computational procedures play an increasingly important role in the stereological analysis of spatial structures and a new sub-discipline, computational stereology, is emarging. Although the chapter is self-contained, it can also be read as a continuation of Kiderlen (2012). In particular, the notation used in Kiderlen (2012) has been adopted in the majority of cases.

1 Rotational integral geometry

Let $\mathcal{K}^d_{\text{conv}}$ denote the set of convex bodies (compact and convex sets) in $\mathbb{R}^d$. In this chapter, we will consider geometric identities of the following general form

$$\int \alpha(K \cap L)\,\mathrm{d}L = \beta(K), \tag{1.1}$$

where α, β are geometrical functionals to be defined more precisely below, $K \in \mathcal{K}^d_{\text{conv}}$ is the spatial object of interest, L is the probe (line, plane, sampling window, ...) and $\mathrm{d}L$ is the element of a rotation invariant measure on the set of probes L. We will mainly focus on geometric identities for k-dimensional planes L in $\mathbb{R}^d$ passing through the origin O (L is a k-dimensional linear subspace in $\mathbb{R}^d$, called a k-subspace in the following). The choice of origin is an important question in applications; in biomedicine, K is typically a cell and O is the nucleus or a nucleolus of the cell.

1.1 Rotational integrals of intrinsic volumes

In this section, rotational integrals of intrinsic volumes will be studied. So α is an intrinsic volume, determined on the section, and the aim is to find the corresponding β. As we shall see, β involves weighted curvature measures.

Recall that for $K \in \mathcal{K}^d_{\text{conv}}$, we can define $d+1$ intrinsic volumes $V_k(K)$, $k = 0,\dots,d$. We have

$$\begin{aligned} V_d(K) &= \text{ volume (Lebesgue measure) of } K \\ V_{d-1}(K) &= 2^{-1} \times \text{ surface area of } K \\ V_0(K) &= \text{ the Euler-Poincaré characteristic of } K \end{aligned}$$

For non-empty $K \in \mathcal{K}^d_{\text{conv}}$, V_0 is thus identically equal to 1. The intrinsic volumes can be extended to larger set classes for which V_0 contains interesting topological information.

The intrinsic volumes are examples of real-valued valuations on $\mathbb{R}^d$. They are motion invariant and continuous with respect to the Hausdorff metric. Recall that a real-valued valuation on $\mathbb{R}^d$ is a mapping $f : \mathcal{K}^d_{\text{conv}} \to \mathbb{R}$ satisfying

$$f(K \cup M) + f(K \cap M) = f(K) + f(M),$$

whenever $K, M, K \cup M \in \mathcal{K}^d_{\text{conv}}$. Hadwiger's famous characterization theorem states that any motion invariant, continuous valuation is a linear combination of intrinsic volumes. For more details, see Kiderlen (2012); Schneider and Weil (2008) and references therein.

For $k = 0,\dots,d-1$, $V_k(K)$ can be expressed as integral with respect to principal curvatures. Assume for simplicity of presentation that K is a compact d-dimensional C^2 manifold with boundary. Then, for $k = 0,\dots,d-1$,

$$V_k(K) = \frac{1}{\omega_{d-k}} \int_{\partial K} \sum_{|I|=d-1-k} \prod_{i \in I} \kappa_i(x)\, \mathcal{H}^{d-1}(\mathrm{d}x), \tag{1.2}$$

where $\omega_k = 2\pi^{k/2}/\Gamma(k/2)$ is the surface area of the unit sphere in $\mathbb{R}^k$, ∂K is the boundary of K, the sum runs over all subsets $\{1,\dots,d-1\}$ with $d-1-k$ elements, $\kappa_i(x)$, $i = 1,\dots,d-1$, are the principal curvatures at $x \in \partial K$ and $\mathcal{H}^{d-1}$ is $(d-1)$-dimensional Hausdorff measure. For $k = d-1$, (1.2) reduces to $V_{d-1}(K) = \frac{1}{2}\mathcal{H}^{d-1}(\partial K)$.

The classical Crofton formula relates intrinsic volumes defined on k-dimensional affine subspaces to intrinsic volumes of the original set

$$\int_{\mathcal{E}^d_k} V_j(K \cap E)\,\mathrm{d}E = c^{k,d-k+j}_{j,d} V_{d-k+j}(K), \qquad 0 \le j \le k \le d, \tag{1.3}$$

cf. Kiderlen (2012, Theorem 2.4). Here, $\mathcal{E}_k^d$ is the set of k-dimensional affine subspaces in $\mathbb{R}^d$, called *k-flats* in the following. Any $E \in \mathcal{E}_k^d$ is of the form $E = x + L$, where L is the parallel k-subspace and $x \in L^\perp$. Furthermore, $\mathrm{d}E = \nu_{d-k}(\mathrm{d}x)\,\mathrm{d}L$, where $\mathrm{d}L$ is the element of the rotation invariant probability measure on the set $\mathcal{L}_k^d$ of k-subspaces in $\mathbb{R}^d$ and ν_{d-k} is the Lebesgue measure on $L^\perp$. The explicit form of the known constant is

$$c_{j,d}^{k,d-k+j} = \frac{k!\tau_k\,(d-k+j)!\tau_{d-k+j}}{j!\tau_j\,d!\tau_d},$$

where $\tau_d = \pi^{d/2}/\Gamma(1+\frac{d}{2})$ is the volume of the unit ball in $\mathbb{R}^d$, cf. Kiderlen (2012, (2.3)). Note that for $j = k$, the Crofton formula relates Lebesgue measure on sections $K \cap E$ to Lebesgue measure of the original set K. Likewise, for $j = k-1$, sectional surface area is related to the surface area of K.

Note that in order to ease the reading of this chapter as a continuation of Kiderlen (2012), we use above and throughout this chapter the normalized version of the rotation invariant measure on $\mathcal{L}_k^d$ which is a probability measure.

In rotational integral geometry, the interest is instead in rotational averages of intrinsic volumes

$$\int_{\mathcal{L}_k^d} V_j(K \cap L)\,\mathrm{d}L = ?, \qquad 0 \le j \le k \le d. \tag{1.4}$$

These integrals are valuations on $\mathbb{R}^d$. They are rotation invariant, but typically not translation invariant.

Let us first consider the case $j = k$. This is the simplest case where Lebesgue measure is measured on the section. For $k = 1, \ldots, d$, we have

$$\int_{\mathcal{L}_k^d} V_k(K \cap L)\,\mathrm{d}L = \frac{\Gamma(d/2)}{\pi^{(d-k)/2}\Gamma(k/2)} \int_K |x|^{-(d-k)}\,\nu_d(\mathrm{d}x). \tag{1.5}$$

The proof of this result is based on the Blaschke-Petkantschin formula. This formula exists in many versions. Generally, the Blaschke-Petkantschin formula concerns a decomposition of a product of Hausdorff measures, see Jensen (1998, Theorem 5.6). Here, we only need the decomposition of a single copy of Lebesgue measure. In this case, the Blaschke-Petkantschin formula takes the following form

$$\int_{\mathbb{R}^d} f(x)\,\nu_d(\mathrm{d}x) = \frac{\pi^{(d-k)/2}\Gamma(k/2)}{\Gamma(d/2)} \int_{\mathcal{L}_k^d} \int_L |x|^{d-k}\,\nu_k(\mathrm{d}x)\,\mathrm{d}L,$$

for any non-negative measurable function f on $\mathbb{R}^d$, see Jensen (1998, Proposition 4.5). For $k = 1$ (line sections), the Blaschke-Petkantschin formula is simply polar decomposition in $\mathbb{R}^d$, see also Kiderlen (2012, Section 2.1.2). Note that for $j = k = 0$, (1.4) reduces to

$$\int_{\mathcal{L}_0^d} V_0(K \cap L)\,\mathrm{d}L = \mathbf{1}_K(O).$$

Example 1.1. For $d = 3$ and $k = 2$, we get, cf. (1.5),

$$\int_{\mathcal{L}_2^3} \mathrm{area}(K \cap L)\,\mathrm{d}L = \beta(K),$$

where

$$\beta(K) = \frac{1}{2}\int_K |x|^{-1}\,\nu_3(\mathrm{d}x). \qquad \square$$

The situation is much more complicated, when $j < k$. Assume for simplicity of the presentation that K is a compact d–dimensional C^2 manifold with boundary. Then, under mild regularity conditions,

$$\int_{\mathcal{L}_k^d} V_j(K\cap L)\,\mathrm{d}L = \int_{\partial K} |x|^{-(d-k)} \sum_{|I|=k-1-j} w_{I,k,j}(x)\prod_{i\in I}\kappa_i(x)\,\mathcal{H}^{d-1}(\mathrm{d}x), \tag{1.6}$$

$0 \le j < k \le d$. The sum runs over all subsets of $\{1,\dots,d-1\}$ with $k-1-j$ elements and the $w_{I,k,j}$s are weight functions involving hypergeometric functions. In 2008, this result was published by Jensen and Rataj (2008). Here, the result was established for the more general set class consisting of sets with positive reach. The proof involves extensive geometric measure theory.

Very recently, the explicit form of the weight functions $w_{I,k,j}$ has been published (Auneau-Cognacq et al., 2012). If K is a ball centred at the origin O, then the $w_{I,k,j}$s are constant and $|x|$ is also constant when $x \in \partial K$. We are back to the classical Crofton formula (1.3). Generally, the $w_{I,k,j}$s depend on the angle between x and the outer unit normal $u(x)$ at $x \in \partial K$, *and* the angle between x and the subspace spanned by the principal directions with indices outside I. In Auneau-Cognacq et al. (2012), it is shown for $j < k$ that

$$\int_{\mathcal{L}_k^d} V_j(K\cap L)\,\mathrm{d}L$$

can also be expressed as an integral with respect to flag measures.

The special case $j = k-1$ gives rise to some simplifications of (1.6), see e.g. Jensen and Rataj (2008, Section 4.1). When $j = k-1$, $I = \emptyset$, the sum on the right-hand side of (1.6) has only one element and the curvature product disappears. The following result holds for the rotational average of the sectional surface area

$$\begin{aligned}\int_{\mathcal{L}_k^d} & V_{k-1}(K\cap L)\,\mathrm{d}L \\ &= \frac{1}{2}\frac{\Gamma(d/2)}{\pi^{(d-k)/2}\Gamma(k/2)}\int_{\partial K} |x|^{-(d-k)} F_{-\frac{1}{2},\frac{d-k}{2};\frac{d-1}{2}}(\sin^2\beta(x))\,\mathcal{H}^{d-1}(\mathrm{d}x),\end{aligned} \tag{1.7}$$

where F is a hypergeometric function and $\beta(x)$ is the angle between $x \in \partial K$ and the unique outer unit normal $u(x)$ to the boundary at $x \in \partial K$ (unique because of the smoothness condition).

The class of hypergeometric functions is parametrized by three parameters and has well-known series expansions as well as integral representations. In particular, we have for $0 < \beta < \gamma$ the following integral representation

$$F_{\alpha,\beta;\gamma}(z) = \frac{1}{B(\beta,\gamma-\beta)}\int_0^1 (1-zy)^{-\alpha} y^{\beta-1}(1-y)^{\gamma-\beta-1}\,\mathrm{d}y. \tag{1.8}$$

Example 1.2. For $d = 3$ and $k = 2$, we find, using (1.8),

$$F_{-\frac{1}{2},\frac{d-k}{2};\frac{d-1}{2}}(\sin^2\beta(x)) = \frac{2}{\pi}\int_0^{\pi/2}(1-\sin^2\beta(x)\sin^2\varphi)^{1/2}\mathrm{d}\varphi$$
$$= \frac{2}{\pi}E(|\sin\beta(x)|,\pi/2),$$

where E is the elliptic integral of the second kind. We find, cf. (1.7),

$$\int_{\mathcal{L}_2^3}\text{length}(\partial K\cap L)\,\mathrm{d}L = \beta(K),$$

where

$$\beta(K) = \frac{1}{\pi}\int_{\partial K}|x|^{-1}E(|\sin\beta(x)|,\pi/2)\,\mathcal{H}^2(\mathrm{d}x).$$

□

1.2 Intrinsic volumes as rotational integrals

In this section, we want to study the 'opposite/inverse' problem of determining the measurement in the section with rotational integral equal to a given intrinsic volume. So now β is an intrinsic volume and the aim is to find α such that (1.1) is satisfied. This problem has been studied in detail in Auneau and Jensen (2010); Gual-Arnau et al. (2010).

More specifically, we want to find a functional $\alpha_{k,j}$, satisfying the following rotational integral equation

$$\int_{\mathcal{L}_k^d}\alpha_{k,j}(K\cap L)\,\mathrm{d}L = V_{d-k+j}(K), \tag{1.9}$$

$k = 1,\ldots,d$, $j = 1,\ldots,k$. From an applied point of view, this question is more interesting than the one studied in the previous section, because $\alpha_{k,j}$ is then the measurement to be performed in the section. This measurement has a rotational average equal to the intrinsic volume considered and can be used to estimate the intrinsic volume in question. Further details will be given in Section 2.

Let us first consider a simple example in $\mathbb{R}^2$ with $d = 2$ and $j = k = 1$. The aim is then to find a functional $\alpha_{1,1}$ such that

$$\int_{\mathcal{L}_1^2}\alpha_{1,1}(K\cap L)\,\mathrm{d}L = \text{area}(K). \tag{1.10}$$

It is easy to find a solution to this problem. Consider an infinitesimal neighbourhood of $x \in X$ of area $\nu_2(\mathrm{d}x)$. Transforming to polar coordinates in $\mathbb{R}^2$, $x = (r\cos\theta, r\sin\theta)$, gives us the following decomposition of area measure in the plane

$$\nu_2(\mathrm{d}x) = |r|\,\mathrm{d}r\,\mathrm{d}\theta, \tag{1.11}$$

$r \in \mathbb{R}$, $\theta \in [0,\pi)$. Identifying θ with the line L passing through the origin, having an angle θ with a fixed axis, we have $\mathrm{d}L = \mathrm{d}\theta/\pi$, and (1.11) can equivalently be expressed as

$$\nu_2(\mathrm{d}x) = \pi|x|\,\nu_1(\mathrm{d}x)\,\mathrm{d}L.$$

It follows that

$$\alpha_{1,1}(K \cap L) = \pi \int_{K \cap L} |x| \, \nu_1(\mathrm{d}x)$$

is a solution to (1.10).

A solution to the general problem of finding a functional $\alpha_{k,j}$ satisfying (1.9) can be derived by combining the classical Crofton formula with another version of the Blaschke-Petkantschin formula, see Kiderlen (2012, Theorem 2.7),

$$\int_{\mathcal{E}_r^d} f(E)\,\mathrm{d}E = \frac{\omega_{d-r}}{\omega_{k-r}} \int_{\mathcal{L}_k^d} \int_{\mathcal{E}_r^L} f(E) d(O,E)^{d-k} \,\mathrm{d}E\,\mathrm{d}L, \tag{1.12}$$

where $1 \le r < k \le d-1$, f is a non-negative measurable function on $\mathcal{E}_r^d$ and $\mathcal{E}_r^L$ is the set of r-flats contained in $L \in \mathcal{L}_k^d$.

The general solution to (1.9) is given in the proposition below.

Proposition 1.3 (Auneau and Jensen (2010); Gual-Arnau et al. (2010))**.** *Let $M \in \mathcal{K}_{\mathrm{conv}}^L$ be a compact and convex subset of $L \in \mathcal{L}_k^d$. For $k = 1,\dots,d$, $j = 1,\dots,k$, the functional*

$$\alpha_{k,j}(M) = \frac{\omega_{d-k+1}}{\omega_1} (c_{j-1,d}^{k-1,d-k+j})^{-1} \int_{\mathcal{E}_{k-1}^L} d(O,E)^{d-k} V_{j-1}(M \cap E)\,\mathrm{d}E$$

is a solution to (1.9).

Proof. Using the Blaschke-Petkantschin formula (1.12), we find

$$\begin{aligned}
&\int_{\mathcal{L}_k^d} \alpha_{k,j}(K \cap L)\,\mathrm{d}L \\
&= \frac{\omega_{d-k+1}}{\omega_1} (c_{j-1,d}^{k-1,d-k+j})^{-1} \int_{\mathcal{L}_k^d} \int_{\mathcal{E}_{k-1}^L} d(O,E)^{d-k} V_{j-1}(K \cap L \cap E)\,\mathrm{d}E\,\mathrm{d}L \\
&= \frac{\omega_{d-k+1}}{\omega_1} (c_{j-1,d}^{k-1,d-k+j})^{-1} \int_{\mathcal{L}_k^d} \int_{\mathcal{E}_{k-1}^L} d(O,E)^{d-k} V_{j-1}(K \cap E)\,\mathrm{d}E\,\mathrm{d}L \\
&= (c_{j-1,d}^{k-1,d-k+j})^{-1} \int_{\mathcal{E}_{k-1}^d} V_{j-1}(K \cap E)\,\mathrm{d}E \\
&= V_{d-k+j}(K).
\end{aligned}$$

At the last equality sign, we have used the Crofton formula (1.3). □

Example 1.4. For $d = 3$ and $j = k = 2$, we get

$$\int_{\mathcal{L}_2^3} \alpha_{2,2}(K \cap L)\,\mathrm{d}L = \nu_3(K),$$

where

$$\alpha_{2,2}(K \cap L) = \pi \int_{\mathcal{E}_1^L} d(O,E)\,\mathrm{length}\,(K \cap E)\,\mathrm{d}E.$$

Furthermore, for $d = 3$, $j = 1$ and $k = 2$, we get

$$\int_{\mathcal{L}_2^3} \alpha_{2,1}(K \cap L)\,\mathrm{d}L = \tfrac{1}{2}\,\mathrm{surface\ area}\,(K),$$

where

$$\alpha_{2,1}(K\cap L) = 2\pi \int_{\mathcal{E}_1^L} d(O,E)\,\mathbf{1}\{K\cap E\neq\emptyset\}\,\mathrm{d}E.$$

It was shown in Auneau and Jensen (2010) that for $j=k$ and $j=k-1$ the functional $\alpha_{k,j}$ can be considerably simplified and given in more explicit form. The result is presented in the corollary below.

Corollary 1.5. *Let the situation be as in Proposition 1.3. Suppose that $M\in\mathcal{K}^L_{\text{conv}}$ is a compact k-dimensional C^2 manifold with boundary. Then,*

$$\alpha_{k,k}(M) = \frac{\pi^{(d-k)/2}\Gamma(k/2)}{\Gamma(d/2)}\int_M |z|^{d-k}\,\nu_k(\mathrm{d}z)$$

and

$$\alpha_{k,k-1}(M) = \frac{1}{2}\frac{\pi^{(d-k)/2}\Gamma(k/2)}{\Gamma(d/2)}\int_{\partial M} |z|^{d-k} F_{-\frac{1}{2},-\frac{d-k}{2};\frac{k-1}{2}}(\sin^2(\beta(z)))\,\mathcal{H}^{k-1}(\mathrm{d}z),$$

where $\beta(z)$ is the angle between $z\in\partial M$ and the unique outer unit normal $u(z)$ to the boundary of M at $z\in\partial M$.

Proof. Using that $E=L+x$, where $x\in L^\perp$, we find

$$\begin{aligned}
\frac{\Gamma((d-k+1)/2)}{\pi^{(d-k+1)/2}}\alpha_{k,k}(M) &= \int_{\mathcal{E}^L_{k-1}} d(O,E)^{d-k}V_{k-1}(M\cap E)\,\mathrm{d}E\\
&= \int_{\mathcal{L}^k_{k-1}}\int_{L^\perp} |x|^{d-k}V_{k-1}(M\cap(L+x))\,\nu_1(\mathrm{d}x)\,\mathrm{d}L\\
&= \int_{\mathcal{L}^k_{k-1}}\int_{L^\perp}\int_{M\cap(L+x)} |x|^{d-k}\,\nu_{k-1}(\mathrm{d}y)\,\nu_1(\mathrm{d}x)\,\mathrm{d}L\\
&= \int_{\mathcal{L}^k_{k-1}}\int_M |p(z|L^\perp)|^{d-k}\,\nu_k(\mathrm{d}z)\,\mathrm{d}L\\
&= \int_M |z|^{d-k}\Big(\int_{\mathcal{L}^k_{k-1}} \frac{|p(z|L^\perp)|^{d-k}}{|z|^{d-k}}\,\mathrm{d}L\Big)\nu_k(\mathrm{d}z)\\
&= \int_M |z|^{d-k}\Big(\frac{1}{B(\frac{1}{2},\frac{k-1}{2})}\int_0^1 y^{\frac{d-k-1}{2}}(1-y)^{\frac{k-3}{2}}\,\mathrm{d}y\Big)\nu_k(\mathrm{d}z).
\end{aligned}$$

At the last equality sign, we have used Jensen (1998, Proposition 3.9). The result concerning $\alpha_{k,k}$ now follows immediately.

The result concerning $\alpha_{k,k-1}$ is more difficult to show. The details can be found in Auneau and Jensen (2010). Let us here just give a proof sketch. In Auneau and Jensen (2010), it is shown that

$$\frac{\Gamma((d-k+1)/2)}{\pi^{(d-k+1)/2}}\cdot c^{k-1,d-1}_{k-2,d}\cdot\alpha_{k,k-1}(M) = \frac{1}{2}\int_{\partial M}\int_{\mathcal{L}^k_{k-1}} |p(u(z)|L)||p(z|L^\perp)|^{d-k}\,\mathrm{d}L\,\mathcal{H}^{k-1}(\mathrm{d}z).$$

The result now follows if we use the following result proved in Auneau and Jensen (2010). For x and y unit vectors in $L \in \mathcal{L}_k^d$ and non-negative integers n, m, we have

$$\int_{\mathcal{L}_{k-1}^k} |p(x|L)|^m \, |p(y|L^\perp)|^n \mathrm{d}L = \frac{\omega_{k-1}}{\omega_k} B\Big(\frac{n+1}{2}, \frac{m+k-1}{2}\Big) F_{-\frac{m}{2},-\frac{n}{2};\frac{k-1}{2}}(\sin^2 \angle(x,y)).$$

□

In this section we have found a functional $\alpha_{k,j}$ satisfying the rotational integral equation (1.9). A natural question to ask is whether $\alpha_{k,j}$ is unique. If a solution is seeked among rotation invariant functionals only, this is indeed the case for $j = k = 1$, cf. Kiderlen and Jensen (2013). It is an open question whether uniqueness holds for general j and k.

1.3 Rotational integral geometry of Minkowski tensors

In this section, we will extend the results obtained so far to tensor valuations. These results are very recent (Auneau-Cognacq et al., 2013). We will define so-called integrated Minkowski tensors for which a genuine rotational Crofton formula holds. As we shall see, using integrated Minkowski tensors, the two problems of finding (1) rotational averages of intrinsic volumes and (2) expressing intrinsic volumes as rotational integrals can be given a common formulation.

For non-negative integers r and s, $k = 0, \ldots, d-1$, the Minkowski tensors are

$$\Phi_{k,r,s}(K) := \frac{\omega_{d-k}}{r!\, s!\, \omega_{d-k+s}} \int_{\mathbb{R}^d \times S^{d-1}} x^r u^s \, \Lambda_k(K, \mathrm{d}(x,u)) \text{ (surface tensor)}$$

$$\Phi_{d,r,0}(K) := \frac{1}{r!} \int_K x^r \, \nu_d(\mathrm{d}x) \text{ (volume tensor)}$$

Here, x^r is the symmetric tensor of rank r determined by x, while $x^r u^s$ is the symmetric tensor product of x^r and u^s. Furthermore, $\Lambda_k(K,\cdot)$ is the kth support measure or generalized curvature measure of K, $k = 0, \ldots, d-1$. The support measure Λ_k is concentrated on the normal bundle $\operatorname{Nor} K$ of K which consists of all pairs (x,u) where $x \in \partial K$ and u is an outer unit normal vector of K at x. The rank of $\Phi_{k,r,s}(K)$ is $r+s$. If K is smooth such that there is a unique outer unit normal $u(x)$ for each $x \in \partial K$, then the surface tensors can be expressed as follows

$$\Phi_{k,r,s}(K) = \frac{1}{r! s! \omega_{d-k+s}} \int_{\partial K} x^r u(x)^s \sum_{|I|=d-1-k} \prod_{i \in I} \kappa_i(x) \mathcal{H}^{d-1}(\mathrm{d}x),$$

$k = 0, \ldots, d-1$, r, s non-negative integers.

For $r = s = 0$, we have $\Phi_{k,0,0}(K) = V_k(K)$, the kth intrinsic volume, $k = 0, \ldots, d$. Otherwise, $\Phi_{k,r,s}(K)$ carries interesting information about the position, shape and orientation of K, cf. e.g. Beisbart et al. (2002, 2006); Schröder-Turk et al. (2011a,b). The normalized rank 1 tensor $\Phi_{d,1,0}(K)/\nu_d(K)$ is equal to the usual centre of gravity of K while $\Phi_{d-1,1,0}(K)/V_{d-1}(K)$ is a boundary centre of gravity. Minkowski tensors of rank two and higher provide additional information about the shape and the orientation of K. For further details, see Jensen and Ziegel (2012) and references therein.

For the development of rotational integral geometry of Minkowski tensors, we will now introduce the integrated Minkowski tensors. These tensors are weighted integrals of Minkowski tensors defined on lower-dimensional k-flats.

Definition 1.6. *For $0 \leq j < k < d$, $t > k-d$ and non-negative integers r and s, the integrated Minkowski tensors are*

$$\Phi_{j,r,s}^{k,t}(K) := \int_{\mathcal{E}_k^d} \Phi_{j,r,s}^{(E)}(K \cap E)\, d(O,E)^t \, \mathrm{d}E,$$

and

$$\Phi_{k,r,0}^{k,t}(K) := \int_{\mathcal{E}_k^d} \Phi_{k,r,0}^{(E)}(K \cap E)\, d(O,E)^t \, \mathrm{d}E,$$

where the integrands $\Phi_{j,r,s}^{(E)}(K \cap E)$ and $\Phi_{k,r,0}^{(E)}(K \cap E)$ are calculated relative to E. □

The condition $t > k-d$ ensures that $\Phi_{j,r,s}^{k,t}(K)$ is well-defined. The integrated Minkowski tensors defined in Auneau-Cognacq et al. (2013) are identical to those given in Definition 1.6, up to multiplication by the constant

$$c_{d,k} = \omega_d \cdots \omega_{d-k+1}/[\omega_k \cdots \omega_1].$$

There are a number of interesting special cases of integrated Minkowski tensors. Using Definition 1.6 for $r = s = t = 0$ we have

$$\Phi_{j,0,0}^{k,0}(K) = c_{j,d}^{k,d-k+j}\, V_{d-k+j}(K), \;\; 0 \leq j \leq k < d \quad \text{(classical Crofton formula)}$$

More generally, using Hug et al. (2008, Theorem 2.4 and 2.5), we find

$$\Phi_{j,r,s}^{k,0}(K) = c_{d,k,j,s}\, \Phi_{d-k+j,r,s}(K), \;\; 0 \leq j < k < d, s = 0,1, \tag{1.13}$$

$$\Phi_{k,r,0}^{k,0}(K) = \Phi_{d,r,0}(K), \;\; 0 < k < d. \tag{1.14}$$

Here,

$$c_{d,k,j,s} = c_{j,d}^{k,d-k+j} \frac{\omega_{j+2}}{\omega_{j+s+2}} \frac{\omega_{d-k+j+s+2}}{\omega_{d-k+j+2}}.$$

In Hug et al. (2008), it is also shown for arbitrary non-negative integers s that $\Phi_{j,r,s}^{k,0}$ is a linear combination of Minkowski tensors.

The integrated Minkowski tensors obey a genuine rotational Crofton formula.

Proposition 1.7. (Rotational Crofton formula) *For $0 \leq j < k < p \leq d$, $t > k-d$ and non-negative integers r and s, we have*

$$\Phi_{j,r,s}^{k,t}(K) = \frac{\omega_{d-k}}{\omega_{p-k}} \int_{\mathcal{L}_p^d} \Phi_{j,r,s}^{k,d-p+t}(K \cap L)\, \mathrm{d}L. \tag{1.15}$$

For $j = k$, (1.15) *holds for $s = 0$.*

Proof. We use (1.12) with $r = k$ and $k = p$ and find

$$\begin{aligned}
\Phi_{j,r,s}^{k,t}(K) &= \int_{\mathcal{E}_k^d} \Phi_{j,r,s}^{(E)}(K \cap E) d(O,E)^t \,\mathrm{d}E \\
&= \frac{\omega_{d-k}}{\omega_{p-k}} \int_{\mathcal{L}_p^d} \int_{\mathcal{E}_k^L} \Phi_{j,r,s}^{(E)}(K \cap E) d(O,E)^{d-p+t} \,\mathrm{d}E \,\mathrm{d}L \\
&= \frac{\omega_{d-k}}{\omega_{p-k}} \int_{\mathcal{L}_p^d} \Phi_{j,r,s}^{k,d-p+t}(K \cap L) \,\mathrm{d}L.
\end{aligned}$$

The second statement is proved in exactly the same manner. □

By choosing the parameters in the rotational Crofton formula appropriately, either the left-hand side or the right-hand side of the formula becomes a classical Minkowski tensor.

Corollary 1.8. (Rotational averages of Minkowski tensors) *For $s \in \{0,1\}$ and $t = p-d$, we have*

$$\int_{\mathcal{L}_p^d} \Phi_{m,r,s}^{(L)}(K \cap L) \,\mathrm{d}L = c_{p,p-q,m-q,s}^{-1} \frac{\omega_q}{\omega_{d-(p-q)}} \Phi_{m-q,r,s}^{p-q,p-d}(K), \tag{1.16}$$

for $0 < q \le m < p \le d$.

If $m = p$, then $s = 0$, and we get

$$\int_{\mathcal{L}_p^d} \Phi_{p,r,0}^{(L)}(K \cap L) \,\mathrm{d}L = \frac{\omega_q}{\omega_{d-(p-q)}} \Phi_{p-q,r,0}^{p-q,p-d}(K), \tag{1.17}$$

for $0 < q < p \le d$.

Proof. Combining (1.13) and (1.15), we find

$$\begin{aligned}
\int_{\mathcal{L}_p^d} \Phi_{m,r,s}^{(L)}(K \cap L) \,\mathrm{d}L &= c_{p,p-q,m-q,s}^{-1} \int_{\mathcal{L}_p^d} \Phi_{m-q,r,s}^{p-q,0}(K \cap L) \,\mathrm{d}L \\
&= c_{p,p-q,m-q,s}^{-1} \frac{\omega_q}{\omega_{d-(p-q)}} \Phi_{m-q,r,s}^{p-q,p-d}(K).
\end{aligned}$$

The second statement is proved in exactly the same manner. □

Note that for $r = s = 0$, the left-hand sides of (1.16) and (1.17) are rotational averages of intrinsic volumes, see Section 1.1 and Auneau-Cognacq et al. (2012); Jensen and Rataj (2008).

As we shall see, it is more interesting for applications in local stereology to try to find the functional defined on the subspace L_p whose rotational average equals a given classical Minkowski tensor. This problem can again be solved for $s \in \{0,1\}$ by combining the rotational Crofton formula with equations (1.13) and (1.14).

Corollary 1.9. (Minkowski tensors as rotational averages) *For $s \in \{0,1\}$ and $t = 0$, we have*

$$\Phi_{d+m-p,r,s}(K) = c_{d,p-q,m-q,s}^{-1} \frac{\omega_{d-(p-q)}}{\omega_q} \int_{\mathcal{L}_p^d} \Phi_{m-q,r,s}^{p-q,d-p}(K \cap L) \,\mathrm{d}L, \tag{1.18}$$

for $0 < q \leq m < p \leq d$.

If $m = p$, *then* $s = 0$, *and we get*

$$\Phi_{d,r,0}(K) = \frac{\omega_{d-(p-q)}}{\omega_q} \int_{\mathcal{L}_p^d} \Phi_{p-q,r,0}^{p-q,d-p}(K \cap L)\,\mathrm{d}L, \tag{1.19}$$

for $0 < q < p \leq d$.

Proof. Combining (1.13) and (1.15), we find

$$\begin{aligned} \int_{\mathcal{L}_p^d} \Phi_{m-q,r,s}^{p-q,d-p}(K \cap L)\,\mathrm{d}L &= \frac{\omega_q}{\omega_{d-(p-q)}} \Phi_{m-q,r,s}^{p-q,0}(K) \\ &= \frac{\omega_q}{\omega_{d-(p-q)}} c_{d,p-q,m-q,s} \Phi_{d+m-p,r,s}(K). \end{aligned}$$

The second statement is proved in exactly the same manner. □

For $r = s = 0$ and $q = 1$, the result in Corollary 1.9 reduces to the main result in Auneau and Jensen (2010), see Proposition 1.3.

It is clearly of interest to study what kind of geometric information the integrated Minkowski tensors carry about the original set K. In the proposition below, we give such geometric interpretation for $\Phi_{k,r,0}^{k,t}$ and $\Phi_{d-2,r,0}^{d-1,t}$. For a proof, the reader is referred to Auneau-Cognacq et al. (2013).

Proposition 1.10. *For* $0 < k < d$, $t > k - d$ *and a non-negative integer* r

$$\Phi_{k,r,0}^{k,t}(K) = \frac{1}{r!} \frac{\Gamma(\frac{t+d-k}{2})\Gamma(\frac{d}{2})}{\Gamma(\frac{t+d}{2})\Gamma(\frac{d-k}{2})} \int_K x^r |x|^t \, \nu_d(\mathrm{d}x). \tag{1.20}$$

Furthermore, if K *is a compact* d*-dimensional* C^2 *manifold with boundary, then for* $t > 0$ *and a non-negative integer* r

$$\Phi_{d-2,r,0}^{d-1,t}(K) = \frac{\omega_{d-1}}{2r!\omega_d} B\left(\tfrac{t+1}{2}, \tfrac{d}{2}\right) \times \int_{\partial K} x^r |x|^t F_{-\frac{1}{2},-\frac{t}{2};\frac{d-1}{2}}(\sin^2 \beta(x))\, \mathcal{H}^{d-1}(\mathrm{d}x). \tag{1.21}$$

In Section 1.2, we studied the functional $\alpha_{k,j}$, see Proposition 1.3. Note that this functional is a special case of an integrated Minkowski tensor since

$$\alpha_{k,j}(M) = \frac{\omega_{d-k+1}}{\omega_1} \left(c_{j-1,d}^{k-1,d-k+j}\right)^{-1} \Phi_{j-1,0,0}^{k-1,d-k}(M),$$

$M \in \mathcal{K}_{\text{conv}}^L$, $L \in \mathcal{L}_k^d$. If we in Proposition 1.10 insert these parameter values, we get the result in Corollary 1.5.

1.4 A principal rotational formula

To the best of our knowledge, a principal rotational formula is still not available in the literature. Focusing on intrinsic volumes, such a formula involves integrals of the form

$$\int_{SO_d} V_k(K \cap RM)\,dR, \tag{1.22}$$

$k = 0,\dots,d$, where SO_d is the special orthogonal group in $\mathbb{R}^d$, K and M are convex and compact subsets of $\mathbb{R}^d$, and dR is the element of the unique rotation invariant probability measure on SO_d. From an applied point of view such a formula is interesting. Here, K is the unknown spatial structure of interest while M is a known 'sampling window' constructed by the observer. The aim is to get information about K from observation of the intersection of K with a randomly rotated version of M. For $k = d$, (1.22) is equal to

$$\frac{1}{\omega_d}\int_0^\infty r^{-(d-1)}\mathcal{H}^{d-1}(K \cap r\mathbb{S}^{d-1})\mathcal{H}^{d-1}(M \cap r\mathbb{S}^{d-1})\,dr.$$

To see this, we use that

$$\begin{aligned}\int_{SO_d} V_d(K \cap RM)\,dR &= \int_{SO_d}\int_{\mathbb{R}^d} \mathbf{1}_{K\cap RM}(x)\,\nu_d(dx)\,dR\\ &= \int_{\mathbb{R}^d} \mathbf{1}_K(x)\Big[\int_{SO_d} \mathbf{1}_{RM}(x)\,dR\Big]\,\nu_d(dx).\end{aligned}$$

Since

$$\begin{aligned}\int_{SO_d} \mathbf{1}_{RM}(x)\,dR &= \int_{SO_d} \mathbf{1}_M(R^{-1}x)\,dR\\ &= \int_{SO_d} \mathbf{1}_M(Rx)\,dR\\ &= \mathcal{H}^{d-1}(M \cap |x|\mathbb{S}^{d-1})/\mathcal{H}^{d-1}(|x|\mathbb{S}^{d-1})\\ &= |x|^{-(d-1)}\omega_d^{-1}\mathcal{H}^{d-1}(M \cap |x|\mathbb{S}^{d-1}),\end{aligned}$$

we obtain

$$\begin{aligned}\int_{SO_d} V_d(K \cap RM)\,dR &= \frac{1}{\omega_d}\int_K |x|^{-(d-1)}\mathcal{H}^{d-1}(M \cap |x|\mathbb{S}^{d-1})\,\nu_d(dx)\\ &= \frac{1}{\omega_d}\int_0^\infty r^{-(d-1)}\mathcal{H}^{d-1}(K \cap r\mathbb{S}^{d-1})\mathcal{H}^{d-1}(M \cap r\mathbb{S}^{d-1})\,dr.\end{aligned}$$

A result of a similar form involving two terms can be obtained for $k = d-1$. The case of general k is still open.

2 Local stereology

Local stereology is the branch of stereology, dealing with inference about $K \in \mathcal{K}^d_{\mathrm{conv}}$ from sections $K \cap L$, $L \in \mathcal{L}^d_k$, $0 < k < d$. Usually, the set class considered is not restricted to compact and convex subsets of $\mathbb{R}^d$, but we will here focus on such sets for the sake of simplicity of presentation. A model example of application of local stereology is the case when K is a biological cell, studied via sections of the cell with planes passing through a reference point, usually taken to be the cell nucleus or a nucleolus. In the following, we will identify the reference point with the origin O.

The monograph Jensen (1998) is an introduction to local stereology, where the focus is on Hausdorff measures rather than on intrinsic volumes. In Jensen (1998), the local stereological procedures are mainly presented from a design-based point of view, where K is regarded as fixed, while the k-subspace L is isotropic random. See also the recent publication Jensen and Ziegel (2012) where this point of view is taken in relation to estimation of Minkowski tensors.

In this chapter, we will take the dual model-based point of view. We let Z be an isotropic random convex body in $\mathbb{R}^d$ and let $\bar{V}_j(Z) = \mathbf{E}V_j(Z)$, $j = 0, \ldots, d$, denote its mean intrinsic volumes. One of our aims is to use the rotational integral geometric identities, developed in the previous section, to derive unbiased local stereological estimators of the mean intrinsic volumes.

The results in Section 1.1 can be used to relate mean intrinsic volumes $\bar{V}_j(Z \cap L)$ on a k-subspace L to properties of the original random set Z. For this purpose, let

$$\begin{aligned}
\bar{\Phi}_d(Z, A) &= \mathbf{E}\nu_d(Z \cap A), & A &\in \mathcal{B}(\mathbb{R}^d), \\
\bar{\Lambda}_j(Z, A \times B) &= \mathbf{E}\Lambda_j(Z, A \times B), & A &\in \mathcal{B}(\mathbb{R}^d), B \in \mathcal{B}(\mathbb{S}^{d-1}),
\end{aligned}$$

$j = 0, \ldots, d-1$. Here, $\bar{\Lambda}_j(Z, \cdot)$ is the mean jth support measure associated with Z. Note that $\bar{\Phi}_d(Z, \cdot)$ has the following simple expression

$$\bar{\Phi}_d(Z, A) = \int_A p_Z(x)\, \nu_d(\mathrm{d}x), \qquad A \in \mathcal{B}(\mathbb{R}^d),$$

where $p_Z(x) = \mathbf{P}(x \in Z)$, $x \in \mathbb{R}^d$. Using (1.5), we find for $L \in \mathcal{L}_k^d$,

$$\begin{aligned}
\bar{V}_k(Z \cap L) &= \int_{\mathcal{L}_k^d} \mathbf{E}V_k(Z \cap M)\, \mathrm{d}M \\
&= \mathbf{E} \int_{\mathcal{L}_k^d} V_k(Z \cap M)\, \mathrm{d}M \\
&= \mathbf{E} \frac{\Gamma(d/2)}{\pi^{(d-k)/2}\Gamma(k/2)} \int_Z |x|^{-(d-k)}\, \nu_d(\mathrm{d}x) \\
&= \frac{\Gamma(d/2)}{\pi^{(d-k)/2}\Gamma(k/2)} \int_{\mathbb{R}^d} |x|^{-(d-k)}\, \bar{\Phi}_d(Z, \mathrm{d}x).
\end{aligned}$$

At the first equality sign, we have used that V_k and the distribution of Z is invariant under rotations. Likewise, we find for $L \in \mathcal{L}_k^d$, using (1.7),

$$\begin{aligned}
&\bar{V}_{k-1}(Z \cap L) \\
&\quad = \frac{\Gamma(d/2)}{\pi^{(d-k)/2}\Gamma(k/2)} \int_{\mathbb{R}^d \times \mathbb{S}^{d-1}} |x|^{-(d-k)} F_{-\frac{1}{2}, \frac{d-k}{2}; \frac{d-1}{2}}(\sin^2 \angle(x, u))\, \bar{\Lambda}_{d-1}(Z, \mathrm{d}(x, u)).
\end{aligned}$$

The result (1.6) can be used to get a general expression for $\bar{V}_j(Z \cap L)$, $j = 0, \dots, k-1$, as an integral with respect to $\bar{\Lambda}_{d-1}(Z, \cdot)$.

Example 2.1. For $d = 3$ and $k = 2$, we get

$$\overline{\text{area}}(Z \cap L) = \frac{1}{2} \int_{\mathbb{R}^3} |x|^{-1} \, \bar{\Phi}_3(Z, \mathrm{d}x)$$

and

$$\overline{\text{length}}(\partial Z \cap L) = \frac{2}{\pi} \int_{\mathbb{R}^3 \times \mathbb{S}^2} |x|^{-1} E(|\sin \angle(x, u)|, \pi/2) \, \bar{\Lambda}_2(Z, \mathrm{d}(x, u)),$$

see also Example 1.1 and 1.2. □

In order to derive unbiased local stereological estimators of mean intrinsic volumes of the original set Z, we need the rotational integral geometric identities derived in Section 1.2. Using Proposition 1.3, we find for $L \in \mathcal{L}_k^d$

$$\bar{V}_{d-k+j}(Z) = \frac{\omega_{d-k+1}}{\omega_1} \left(c_{j-1,d}^{k-1,d-k+j} \right)^{-1} \int_{\mathcal{E}_{k-1}^L} d(O, E)^{d-k} \bar{V}_{j-1}(Z \cap E) \, \mathrm{d}E, \tag{2.1}$$

$k = 1, \dots, d$, $j = 1, \dots, k$. In the particular case $j = k$, we get, using Corollary 1.5, the more explicit expression

$$\bar{V}_d(Z) = \frac{\pi^{(d-k)/2} \Gamma(k/2)}{\Gamma(d/2)} \int_L |x|^{d-k} \, \bar{\Phi}_k(Z \cap L, \mathrm{d}x). \tag{2.2}$$

It follows that

$$m(Z \cap L) = \frac{\pi^{(d-k)/2} \Gamma(k/2)}{\Gamma(d/2)} \int_{Z \cap L} |x|^{d-k} \, \nu_k(\mathrm{d}x) \tag{2.3}$$

is an unbiased estimator of $\bar{V}_d(Z)$.

Example 2.2. (Local estimation of volume in $\mathbb{R}^3$) Let $d = 3$ and $k = 1$. It follows from (2.3) that for $L_1 \in \mathcal{L}_1^3$

$$m(Z \cap L_1) = 2\pi \int_{Z \cap L_1} |x|^2 \, \nu_1(\mathrm{d}x) \tag{2.4}$$

is an unbiased estimator of the mean volume $\bar{V}_3(Z)$ of Z. This estimator is called the nucleator in the applied literature (Gundersen, 1988) and will here be denoted by $m_{cl_1}(Z \cap L_1)$ (the index cl_1 stands for *classical nucleator* based on observation along 1 line). If $O \in Z$, $Z \cap L_1 = [x_-, x_+]$ is a line segment containing the origin and (2.4) reduces to

$$m_{cl_1}(Z \cap L_1) = \frac{2\pi}{3} (|x_+|^3 + |x_-|^3),$$

cf. Figure 1.

Note that if Z is a ball centred at O with random radius, then $m_{cl_1}(Z \cap L_1)$ is identically equal to the volume of Z. The estimator based on observation along two perpendicular lines

$$m_{cl_2}(Z \cap L_1) = \tfrac{1}{2} [m_{cl_1}(Z \cap L_1) + m_{cl_1}(Z \cap L_1^{\perp})]$$

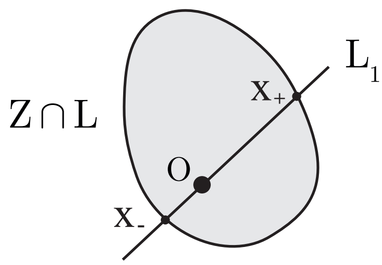

Figure 1: The nucleator estimator requires the measurement of the distance from the origin O to the boundary points x_+ and x_-.

is widely used and highly cited in the biosciences.

For $d = 3$ and $k = 2$, (2.3) leads to an unbiased estimator of $\bar{V}_3(Z)$ based on measurements in a plane L through O. The estimator is called the *integrated nucleator*, cf. Hansen et al. (2011b), and takes the following form

$$m_{int}(Z \cap L) = 2 \int_{Z \cap L} |x| \, \nu_2(\mathrm{d}x).$$

The reason why the estimator is called the integrated nucleator is the following result

$$m_{int}(Z \cap L) = \int_{\mathcal{L}_1^L} m_{cl_1}(Z \cap L_1) \, \mathrm{d}L_1, \tag{2.5}$$

that can be shown, using polar decomposition in the plane L. Recently, Luis M. Cruz-Orive has shown that the integrated nucleator is identical to the so-called *wedge estimator*, see Cruz-Orive (2012). A discretized version of $m_{int}(Z \cap L)$, called the isotropic *rotator*, was introduced already in Jensen and Gundersen (1993) together with another local stereological estimator of volume, the so-called vertical rotator. □

Example 2.3. (Local estimation of surface area in $\mathbb{R}^3$) Let $d = 3$ and consider estimators of the mean surface area $\bar{S}(Z) = 2\bar{V}_2(Z)$. Using (2.1) with $d = 3$, $k = 2$ and $j = 1$, we find that

$$\bar{V}_2(Z) = 2\pi \int_{\mathcal{E}_1^L} d(O, E) \bar{V}_0(Z \cap E) \, \mathrm{d}E.$$

It follows that

$$m(Z \cap L) = 4\pi \int_{\mathcal{E}_1^L} d(O, E) \mathbf{1}\{Z \cap E \neq \emptyset\} \, \mathrm{d}E$$

is an unbiased estimator of $\bar{S}(Z)$.

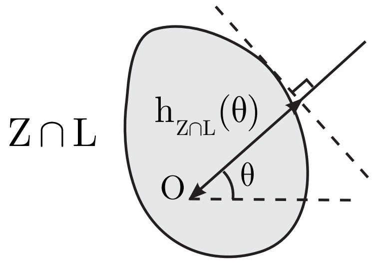

Figure 2: For $\theta \in [0, 2\pi)$, the value $h_{Z\cap L}(\theta)$ of the support function is the distance from the origin O to the touching stipped line.

If $O \in Z$, we can express $m(Z \cap L)$ in a simple way by means of the support function $h_{Z\cap L}$ of $Z \cap L$. (The definition of the support function is illustrated in Figure 2.) We find

$$\begin{aligned} m(Z \cap L) &= 4\pi \int_0^{\pi} \int_{-h_{Z\cap L}(\theta+\pi)}^{h_{Z\cap L}(\theta)} |r| \, \mathrm{d}r \, \frac{\mathrm{d}\theta}{\pi} \\ &= 4 \int_0^{\pi} \Big[\int_0^{h_{Z\cap L}(\theta)} r \, \mathrm{d}r + \int_0^{h_{Z\cap L}(\theta+\pi)} r \, \mathrm{d}r \Big] \mathrm{d}\theta \\ &= 2 \int_0^{2\pi} h_{Z\cap L}(\theta)^2 \, \mathrm{d}\theta. \end{aligned}$$

This representation shows that $m(Z \cap L)$ is equal to four times the area of the flower set associated with $Z \cap L$, defined by

$$F(Z \cap L) := \{ r(\cos\theta, \sin\theta) \,|\, 0 \le r \le h_{Z\cap L}(\theta) \}.$$

This result was first published in Cruz-Orive (2005). The estimator has accordingly been called the *flower estimator*. In Cruz-Orive (2008, 2011), a discretization of $m(Z \cap L)$ based on measurement of the support function in both directions along two perpendicular lines is further discussed. The resulting discretized estimator is called the *pivotal estimator* and is very efficient, see Dvořák and Jensen (2013).

An alternative representation of $m(Z \cap L)$ may be obtained by using the second result of Corollary 1.5 for $d = 3$ and $k = 2$ and the fact that

$$F_{-\frac{1}{2}, -\frac{1}{2}; \frac{1}{2}}(\sin^2 \angle(x,u)) = \cos\angle(x,u) + \angle(x,u) \sin\angle(x,u),$$

cf. e.g. Jensen (1998, p. 146). Using this, the close relation to another estimator of surface area, the *surfactor* (Jensen and Gundersen, 1987), may be seen. For further details, see Jensen and Ziegel (2012, Section 5.1.4). □

Using the results in Section 1.3, we can derive local stereological estimators of Minkowski tensors. For simplicity, we will here focus on the case of volume tensors.

A more comprehensive treatment is given in Jensen and Ziegel (2012). Combining (1.19) and (1.20), we find for $L \in \mathcal{L}_k^d$

$$\bar{\Phi}_{d,r,0}(Z) = \frac{\pi^{(d-k)/2}\Gamma(k/2)}{\Gamma(d/2)} \frac{1}{r!} \int_L x^r |x|^{d-k} \bar{\Phi}_k(Z \cap L, \mathrm{d}x). \tag{2.6}$$

For $r = 0$, the result reduces to (2.2).

Using (2.6), we can construct local stereological estimators of centres of gravity ($r = 1$) and volume tensors of rank two ($r = 2$) that can be used to obtain information about orientation and shape of Z. Below, we only consider the case $r = 1$.

Example 2.4. (Local estimation of centre of gravity in $\mathbb{R}^3$) Let $d = 3$, $r = 1$ and $k = 1$. Then, we find, using (2.6),

$$\bar{\Phi}_{3,1,0}(Z) = 2\pi \int_L x|x|^2 \bar{\Phi}_1(Z \cap L, \mathrm{d}x).$$

It follows that

$$m(Z \cap L) = 2\pi \int_{Z \cap L} x|x|^2 \nu_1(\mathrm{d}x)$$

is an unbiased estimator of $\bar{\Phi}_{3,1,0}(Z)$. If $O \in Z$, then $Z \cap L$ is a line segment $[x_-, x_+]$, containing O. If e is a unit vector spanning L and pointing in the same direction as x_+, then

$$m(Z \cap L) = \frac{\pi}{2}(|x_+|^4 - |x_-|^4)e.$$

Note that if Z is centrally symmetric around O, then $m(Z \cap L) = O$, always. □

The local stereological estimators can be used to analyze a particle population, using local sectional data, thereby providing information about the size, position, orientation and shape of the particles. Let us assume that the particles may be described by a stationary germ-grain model

$$\cup_{i=1}^{\infty}(x_i + Z_i),$$

where $\{x_i\}$ is a stationary point process in $\mathbb{R}^d$ and $\{Z_i\}$ are i.i.d. nonempty, compact and convex random subsets of $\mathbb{R}^d$, independent of $\{x_i\}$. We let Z_0 be a random set with the common distribution of the Z_is, denoted by $\mathbf{Q}$. We will assume that $\mathbf{Q}$ is invariant under rotations in $\mathbb{R}^d$.

Our aim is to estimate the distribution of $\beta(Z_0)$ from local sectional data where β may be an intrinsic volume or, more generally, a Minkowski tensor. Available for observation is a sample of particles $\{x_i + Z_i : x_i \in W\}$ collected in a d-dimensional sampling window W, see Figure 3. We will focus on the situation in optical microscopy, where it is possible to perform measurements on any virtual section $Z_i \cap L$, $L \in \mathcal{L}_k^d$. If α is a rotation invariant functional, satisfying

$$\int_{\mathcal{L}_k^d} \alpha(K \cap L)\,\mathrm{d}L = \beta(K),$$

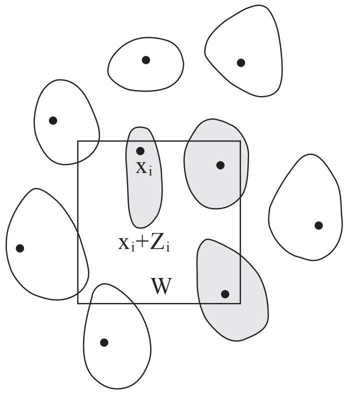

Figure 3: Sampling of particles with reference point in W. Sampled particles are shown grey.

for any $K \in \mathcal{K}^d_{\text{conv}}$, then

$$\bar{\alpha}(Z_0 \cap L) = \int_{\mathcal{L}^d_k} \bar{\alpha}(Z_0 \cap M)\,\mathrm{d}M = \mathbf{E}\Big(\int_{\mathcal{L}^d_k} \alpha(Z_0 \cap M)\,\mathrm{d}M\Big) = \mathbf{E}(\beta(Z_0)) = \bar{\beta}(Z_0).$$

If we let N be the number of sampled particles, then

$$\sum_{x_i \in W} \alpha(Z_i \cap L)/N$$

is a ratio-unbiased estimator of $\bar{\beta}(Z_0)$. If several sections are used per particle Z_i, one may estimate $\beta(Z_i)$ precisely and use the empirical distribution of $\{\hat{\beta}(Z_i) | x_i \in W\}$ as an estimate of the distribution of $\beta(Z_0)$.

Local stereology of spherical particles with non-centrally placed reference point has recently been studied in Thórisdóttir and Kiderlen (2013).

3 Variance reduction techniques

In the previous section, we have used rotational integral geometric identities to develop local stereological procedures for estimating quantitative properties of a spatial structure. The local stereological estimators can be applied without specific shape assumptions but may have a large variance. In this section, we will discuss procedures for reducing the variance of the estimators. Some of the procedures require the use of automatic image analysis. We will focus on the local stereological estimators presented in Examples 2.2 and 2.3 of the previous section.

So, in this section, Z will be an isotropic random convex body in $\mathbb{R}^3$. Let us first consider estimation of the mean volume $\bar{V}_3(Z)$ as described in Example 2.2. We let $L \in \mathcal{L}^3_2$ be a plane through the origin and $L_1 \in \mathcal{L}^L_1$ a line in L through the origin. Since $m_{cl_1}(Z \cap L_1)$

and $m_{cl_1}(Z \cap L_1^\perp)$ are identically distributed, we have

$$\begin{aligned}\mathbf{var}(m_{cl_2}) &= \mathbf{var}(\tfrac{1}{2}[m_{cl_1}(Z \cap L_1) + m_{cl_1}(Z \cap L_1^\perp)]) \\ &= \tfrac{1}{2}[\mathbf{var}(m_{cl_1}) + \mathbf{cov}(m_{cl_1}(Z \cap L_1), m_{cl_1}(Z \cap L_1^\perp))] \\ &\leq \mathbf{var}(m_{cl_1}).\end{aligned}$$

It follows that the variance of the classical nucleator based on observation along two perpendicular lines is smaller than or equal to the variance obtained when just observing along one line.

Because of (2.5), the integrated nucleator m_{int} may be regarded as a classical nucleator based on measurements along an infinite number of lines. As a consequence, the variance of m_{int} is expected to be smaller than or equal to the variance of m_{cl_1} (and m_{cl_2}). A formal argument for this result goes as follows. The identity (2.5) may be regarded as a conditional mean value result, viz.

$$m_{int} = \mathbf{E}(m_{cl_1}(Z \cap L_1)|Z),$$

where the mean value is conditional on Z and with respect to an isotropic line L_1 in the plane L through O, independent of Z. It follows that

$$\begin{aligned}\mathbf{var}(m_{cl_1}) &= \mathbf{var}(\mathbf{E}(m_{cl_1}(Z \cap L_1)|Z)) + \mathbf{E}(\mathbf{var}(m_{cl_1}(Z \cap L_1)|Z)) \\ &= \mathbf{var}(m_{int}) + \mathbf{E}(\mathbf{var}(m_{cl_1}(Z \cap L_1)|Z)) \\ &\geq \mathbf{var}(m_{int}).\end{aligned}$$

Similarly, $\mathbf{var}(m_{cl_2}) \geq \mathbf{var}(m_{int})$.

Because of these variance relations, it appears as an obvious idea to use m_{int} instead of m_{cl_1} or m_{cl_2}. In contrast to the two latter estimators that requires a few distance measurements by an expert, m_{int} needs automatic segmentation of $Z \cap L$. Let $\tilde{Z}_2$ be an estimate of the section $Z \cap L$, obtained by computerized image analysis. The automatic nucleator is now defined as

$$m_{aut} = m_{int}(\tilde{Z}_2).$$

Since the segmentation may not be precise in all cases, an intermediate version may be preferable. An expert supervises the process. If the segmentation is judged satisfactory, m_{aut} is used, otherwise the expert intervenes and determine m_{cl_2} manually. This estimator is called the semi-automatic nucleator and is denoted m_{semi}, cf. Hansen et al. (2011b).

The estimators m_{cl_1}, m_{cl_2} and m_{int} are unbiased while m_{aut} and m_{semi} may be biased. In fact, m_{aut} may be heavily biased if the segmentation is generally unsatisfactory while the bias of m_{semi} is expected to be small because the segmented section $\tilde{Z}_2$ is only used when the segmentation is judged satisfactory by an expert. Also, m_{semi} is expected to be more precise (for instance, in terms of mean square error) than the best manual estimator m_{cl_2}, because m_{semi} only differs from m_{cl_2} when the segmentation is satisfactory and in these cases, the more precise estimator m_{int} is used.

In a concrete study of somastatin positive inhibitory interneurons from transgenic GFP-GAD mice hippocampi, cf. Hansen et al. (2011b), it was found that m_{aut} had a bias of 32 % while m_{semi} only 0.4 %. The relative error ($\sqrt{\text{MSE}}$ / mean) was 0.58, 0.61 and 0.69 for m_{int}, m_{semi} and m_{cl_2}, respectively.

A similar comparative investigation has been performed in Dvořák and Jensen (2013) for the local stereological estimators of mean surface area presented in Example 2.3. The estimator that requires automatic segmentation of the planar section $Z \cap L$ is here the flower estimator. Semi-automatic estimation based on two types of discretizations of the flower estimator, namely the pivotal estimator and the surfactor, has been investigated in Dvořák and Jensen (2013). For ellipsoidal particles, it is shown that the flower estimator is equal to the pivotal estimator based on support function measurements along four perpendicular rays. This makes the pivotal estimator a powerful approximation to the flower estimator. An important decrease in workload may be obtained by using the semi-automatic approach.

4 Computational stereology

Stereology provides information about quantitative properties of spatial structures from observations in lower-dimensional sections of the spatial structure under study. A stereological procedure typically involves the following steps: (1) sampling of blocks to be analyzed, (2) generation of sections through the blocks and (3) analysis of the sampled sections (Baddeley and Jensen, 2005, Chapter 12).

Until recently, stereology has mainly been a 'manual' discipline. Each of the three steps mentioned above has been performed manually by experts and technicians. However, during the last decades, computers have become an increasingly important tool in the stereological analysis of spatial structures, and a new sub-discipline of stereology, computational stereology, is emerging. Computational stereology may be defined as the sub-discipline of stereology that deals with the design of computational procedures that can substitute manual procedures in one of the three steps mentioned above (Rasmusson, 2012).

It is expected that computational stereology will influence the practice in the laboratory. For instance, computational stereology may imply faster execution times compared to existing manual procedures or more efficient probes that require reliable automatic segmentation. Eventually, computational stereology may also affect the advance of theoretical stereology. Computational procedures thus open up the possibility for developing new stereological methods for estimating more complicated quantities than scalar quantities such as volume, surface area, length and number. One obvious example is the Minkowski tensors. On the other hand, a clear definition of computational stereology may make developers of computational image analysis tools realize the importance of 3D interpretations of 2D sections.

Before, images were typically recorded by systematically moving the microscope stage and taking photographs (micrographs) of the generated fields of view in the microscope. Subsequently, the analysis was performed manually on the generated micrographs. Nowadays, computers are used in the acquisition of the images to be analyzed by stereological methods. Such digital images are a prerequisite for any procedure in computational stereology.

The appearance of *whole slide scanners* has been a major advance for computational stereology. Here, the operator delineates the region of interest (ROI) of the sampled section and the whole slide scanner then generates a digital representation of the ROI. It is important that the scanning and storage of the digital images of the sampled sections can be performed without interference by the operator. As a consequence, the operator has the freedom to choose an appropriate time for analysis of the digital images, using developed software.

With digital representations of the sampled sections, it is possible to (1) extend the class of stereological estimators that can be implemented and (2) develop efficient subsampling of the sections under study.

An example of issue 1 relates to the disector that is used for estimating particle number (Kiderlen, 2012, p. 41–42). It is here needed to identify particles in pairs of sections. The manual alignment of the pair of sections may be very time consuming. It is therefore an important advance that this alignment can be performed automatically on the basis of a digital representation of the two sections.

With a digital representation of the sampled sections, it is also possible to implement intelligent non-uniform sampling of fields of view within the section that may result in an important reduction in the variance of stereological estimators (issue 2). The standard procedure has until recently been to use systematic uniform random sampling of fields of view. If the particles (cells) of interest are distributed in an inhomogeneous pattern in the sampled section, this approach may, however, be rather inefficient. In such cases, many fields of view will contain no or very few cells, if systematic uniform random sampling is used. The idea is to use instead non-uniform sampling of fields of view with a probability of selecting a particular field of view that is roughly proportional to the number of cells seen in the field of view. Let the ith field of view contains y_i cells, $i = 1,\ldots,N$, where N is the total number of fields of view. Let $S \subset \{1,\ldots,N\}$ be the random sample of fields of view and p_i the probability that the ith field of view is included in the sample. Provided that $p_i > 0$ whenever $y_i > 0$,

$$\sum_{i \in S} y_i / p_i$$

is an unbiased estimator of the total number of the cells in the section. Typically, the sampling probability p_i is determined automatically from a scan of the section at low magnification, using a colour proportion that is roughly proportional to y_i while the actual counts in the sampled fields of view are determined by an operator at high magnification. If p_i is exactly proportional to y_i, this estimator always gives the right answer. In empirical studies, increase in efficiencies of a factor of 10 compared to ordinary systematic uniform random sampling has been found, see Hansen et al. (2011a) and references therein. In the applied stereological literature, the estimator is called the *proportionator*.

Until recently, there have only been limited interactions between researchers in stereology and image analysis. This situation is very unfortunate, at least for the stereologists, because image analysis may actually be required for implementation of advanced stereological procedures. One example is the semi-automatic procedures described in the previous section of this chapter.

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Bibliography

J. Auneau and E. B. V. Jensen. Expressing intrinsic volumes as rotational integrals. *Adv. Appl. Math.*, 45:1–11, 2010.

J. Auneau-Cognacq, J. Rataj, and E. B. V. Jensen. Closed form of the rotational Crofton formula. *Math. Nachr.*, 285:164–180, 2012.

J. Auneau-Cognacq, J. Ziegel, and E. B. V. Jensen. Rotational integral geometry of tensor valuations. *To appear in Adv. Appl. Math.*, 2013.

A. Baddeley and E. B. V. Jensen. *Stereology for Statisticians*. Number 103 in Monographs on Statistics and Applied Probability. Chapman & Hall/CRC, Boca Raton, 2005.

C. Beisbart, R. Dahlke, K. R. Mecke, and H. Wagner. Vector- and tensor-valued descriptors for spatial patterns. *Lecture Notes in Physics, Springer*, 600:249–271, 2002.

C. Beisbart, M. S. Barbosa, H. Wagner, and L. da F. Costa. Extended morphometric analysis of neuronal cells with Minkowski valuations. *Eur. Phys. J.*, B 52:531–546, 2006.

L. M. Cruz-Orive. A new stereological principle for test lines in three-dimensional space. *J. Microsc.*, 219:18–28, 2005.

L. M. Cruz-Orive. Comparative precision of the pivotal estimators of particle size. *Image Anal. Stereol.*, 27:17–22, 2008.

L. M. Cruz-Orive. Flowers and wedges for the stereology of particles. *J. Microsc.*, 243: 86–102, 2011.

L. M. Cruz-Orive. Uniqueness properties of the invariator, leading to simple computations. *Image Anal. Stereol.*, 31:89–98, 2012.

J. Dvořák and E. B. V. Jensen. On semi-automatic estimation of surface area. *To appear in J. Microsc.*, 2013.

X. Gual-Arnau, L. M. Cruz-Orive, and J. J. Nuno-Ballesteros. A new rotational integral formula for intrinsic volumes in space forms. *Adv. Appl. Math.*, 44:298–308, 2010.

H. J. G. Gundersen. The nucleator. *J. Microsc.*, 151:3–21, 1988.

L. V. Hansen, M. Kiderlen, and E. B. V. Jensen. Image-based empirical importance sampling: an efficient way of estimating intensities. *Scand. J. Statist.*, 38:393–408, 2011a.

L. V. Hansen, J. R. Nyengaard, J. B. Andersen, and E. B. V. Jensen. The semi-automatic nucleator. *J. Microsc.*, 242:206–215, 2011b.

D. Hug, R. Schneider, and R. Schuster. Integral geometry of tensor valuations. *Adv. Appl. Math.*, 41:482–509, 2008.

E. B. Jensen and H. J. G. Gundersen. Stereological estimation of surface area of arbitrary particles. *Acta Stereol.*, 6:25–30, 1987.

E. B. V. Jensen. *Local Stereology*. World Scientific, Singapore, 1998.

E. B. V. Jensen and H. J. G. Gundersen. The rotator. *J. Microsc.*, 170:35–44, 1993.

E. B. V. Jensen and J. Rataj. A rotational integral formula for intrinsic volumes. *Adv. Appl. Math.*, 41:530–560, 2008.

E. B. V. Jensen and J. F. Ziegel. Local stereology of tensors. Technical report, 12-11, Centre for Stochastic Geometry and Advanced Bioimaging, Department of Mathematics, Aarhus University, Denmark. Submitted, 2012.

M. Kiderlen. Introduction into integral geometry and stereology. In E. Spodarev, editor, *Stochastic Geometry, Spatial Statistics and Random Fields: Asymptotic Methods*, number 2068 in Lecture Notes in Mathematics, chapter 2, pages 21–47. Springer, Berlin, 2012.

M. Kiderlen and E. B. V. Jensen. On uniqueness of rotational formulae. Technical report, Centre for Stochastic Geometry and Advanced Bioimaging, Department of Mathematics, Aarhus University, Denmark. In preparation, 2013.

A. Rasmusson. *Contributions to Computational Stereology and Parallel Programming*. PhD Thesis, Department of Computer Science, Aarhus University, Denmark, 2012.

R. Schneider and W. Weil. *Stochastic and Integral Geometry*. Springer, Berlin, 2008.

G. E. Schröder-Turk, S. C. Kapfer, B. Breidenbach, C. Beisbart, and K. Mecke. Tensorial Minkowski functionals and anisotropy measures for planar patterns. *J. Microsc.*, 238: 57–74, 2011a.

G. E. Schröder-Turk, W. Mickel, S. C. Kapfer, M. A. Klatt, F. M. Schaller, M. J. F. Hoffmann, N. Kleppmann, P. Armstrong, A. Inayat, D. Hug, M. Reichelsdorfer, W. Peukert, W. Schwieger, and K. Mecke. Minkowski tensor shape analysis of cellular, granular and porous structures. *Adv. Mater.*, 23:2535–2553, 2011b.

Ó Thórisdóttir and M. Kiderlen. Wicksell's problem in local stereology. *To appear in Adv. Appl. Probab.*, 2013.