LOCAL STEREOLOGY

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Eva B. Vedel Jensen

University of Aarhus

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Preface

The aim of this book is to give a unified exposition of local stereological methods. It is my belief that such a book containing the mathematical and statistical foundations of local stereology is needed since these methods are now in world-wide use in the microscopical study of biological tissue. In many ways this is a very personal book, for a large part based on my own research, and I hope that some of my enthusiasm and joy in working in this area will be acknowledged by the reader.

Local stereology has gradually developed during the last fifteen years, as a product of practical needs from the biologists and new advances in the microscopical observation techniques and in the theoretical foundations of local stereology, integral geometry and geometric probability. Three colleagues have had a profound influence on my engagement in local stereology. Roger Miles wrote a fundamental series of papers about stereology and integral geometry in the seventies and the eighties, partly together with Pamela Davy. His paper *Some new integral geometric formulae, with stochastic applications*, published in *Journal of Applied Probability* in 1979, became especially important since it contained the tools for constructing local estimators of volume, as we simultaneously realized in 1983. The needs from the users of stereology have been realized through my close collaboration with Hans Jørgen G. Gundersen since 1977. I have during the years tried to cope with his never ending series of questions and their solutions occupy a fair part of the book. The mathematical fundament of local stereology has been built together with my former Ph.D. student Kiên Kiêu.

The book is written for researchers, teachers and graduate students in mathematical statistics and probability. In order to reach a broader audience, the book is not only for specialists in stereology, integral geometry and geometric measure theory. In particular, Chapter 1 is an elementary introduction to stereology. Local stereology involves, however, advanced mathematical tools which is an important part of the book too.

Glancing through the book, the reader will realize that this is a book about *geometric sampling*. Chapter 1 contains an exposition of classical global stereology, including Cavalieri's method of volume estimation, estimation via ratios, number estimation using the disector, length and surface area estimation under isotropy, vertical sections. The rest of the book is devoted to local stereology. The mathematical tool for developing local stereological methods is the coarea formula, involving

generalized Jacobians. This transformation formula is presented in Chapter 2 together with many simple geometric examples and also more complicated examples needed in the following chapters. Chapter 3 is a study of the rotation invariant measure on linear subspaces in R^n . Geometric decompositions of the q -fold product of Lebesgue measure are treated in Chapter 4 and generalized to decompositions of Hausdorff measures in Chapter 5. Local slice formulae and some projection formulae are discussed in Chapter 6. Practical aspects of local methods, including their implementation in the microscopical study of biological tissue and some biological applications are presented in Chapter 7 while Chapter 8 discusses the so-called model-based approach, a somewhat misleading terminology since the models considered are of a general non-parametric type.

I want to thank Ole E. Barndorff-Nielsen for originally suggesting to write this book and for following my work with interest. In the academic year 95/96, I lectured on the subjects of the book at the Department of Theoretical Statistics, Institute of Mathematics, University of Aarhus. I am grateful to the 12 students patiently listening to the lectures, reading the lecture notes, discussing the unclear points, doing the exercises, etc. Especially thanks to my Ph.D. student Jørgen Nielsen and to Kristian Stegenborg Larsen and Niels Væver Petersen. I also want to thank Jørgen Hoffmann-Jørgensen for fruitful discussions about the coarea formula and related matters. Comments on earlier drafts by Morten Bech, Hans Jørgen G. Gundersen and Rick Vitale are also gratefully acknowledged. The illustrations have been made with utmost skill and care by Jakob Goldbach, using the programs Adobe Illustrator 6.0 and STRATA STUDIO Pro VERSION 1.75+. Trine Tandrup and Anette Larsen have provided the photographs of biological tissue. Last but not least I want to thank my husband Kaj and my daughter Jane for patiently listening to all my stories during the writing process and for giving me the opportunity to write this book.

Aarhus

Eva B. Vedel Jensen

January 1997

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List of notation

Sets

R^n	n -dimensional Euclidean space. The i 'th coordinate of $x \in R^n$ is denoted x_i or $(x)_i$
R	$= R^1$
O	The origin of R^n
R_+	Positive real numbers
$[a, b]$	Closed, open and half-closed-open intervals, respectively, between $a \in R^n$ and $b \in R^n$, e.g. $[a, b] = \{\alpha a + (1 - \alpha)b : 0 < \alpha \leq 1\}$
(a, b)	
$[a, b)$	
$B_n(x, r)$	Open ball in R^n with centre $x \in R^n$ and radius r
S^{n-1}	The unit sphere in R^n
S_+^{n-1}	$\{\omega \in S^{n-1} : \omega_n > 0\}$
B^n	The unit ball in R^n
L_p	p -subspace; p -dimensional linear subspace of R^n
$\mathcal{L}_p^n$	The set of p -subspaces of R^n
$\mathcal{L}_{p(r)}^n$	The set of p -subspaces of R^n , containing a fixed r -subspace L_r , say. Note that $\mathcal{L}_{p(0)}^n = \mathcal{L}_p^n$
T_p	p -slice of thickness $2t$, i.e. a set of the form $L_p + B_n(O, t)$
T_p^n	The set of p -slices of R^n of thickness $2t$
$T_{p(r)}^n$	The set of p -slices $L_p + B_n(O, t)$ for which $L_p \supseteq L_r$, where L_r is a fixed r -subspace. Note that $T_{p(0)}^n = T_p^n$
G_q	q -grid, i.e. grid of parallel q -dimensional affine subspaces
$\mathcal{G}_q^n$	A set of q -grids in R^n , identical up to rotations and translations
Convex set	A set $X \subseteq R^n$ with the property $[x, y] \subseteq X$ for all $x, y \in X$

Star-shaped set A set $X \subseteq R^n$ is said to be star-shaped relative to $x \in X$, if $[x, y] \subseteq X$ for all $y \in X$

Constants

ω_n The volume (Lebesgue measure) of the unit ball B^n in R^n ,
 $= \pi^{\frac{1}{2}n} \Gamma(1 + \frac{1}{2}n)^{-1}$, cf. Exercise 2.7

σ_n The surface area of the unit sphere S^{n-1} in R^n , $= 2(\pi)^{\frac{1}{2}n} \Gamma(\frac{1}{2}n)^{-1}$, cf. Exercise 2.7

$c(n, p)$ $= \frac{\sigma_n \sigma_{n-1} \cdots \sigma_{n-p+1}}{\sigma_p \sigma_{p-1} \cdots \sigma_1}$

$c(n, 0)$ $\equiv 1$

$b(d, q, n)$ $= \frac{\sigma_{q+d-n+1} \sigma_{n+1}}{\sigma_{d+1} \sigma_{q+1}}$

B_k The k 'th Bernoulli number, $k = 0, 1, \dots$

Inner product and norm

$\langle x, y \rangle$ $= \sum x_i y_i, x, y \in R^n$

$\|x\|$ $= \langle x, x \rangle^{1/2}, x \in R^n$

Concepts relating to linear subspaces

span $\text{span}\{x_1, \dots, x_d\}$ is the linear subspace of R^n , spanned by $x_1, \dots, x_d \in R^n$, i.e. all vectors of the form $\alpha_1 x_1 + \cdots + \alpha_d x_d$, where $\alpha_i \in R, i = 1, \dots, d$

$L^\perp$ The orthogonal complement of the linear subspace L of R^n , $x \in L^\perp$ if and only if $\langle x, y \rangle = 0$ for all $y \in L$

$\dim L$ Dimension of L

$L \oplus M$ Orthogonal sum of the linear subspaces L and M of R^n , i.e. $L \oplus M$ is the sum of L and M , and L and M are orthogonal

$L \ominus M$ Orthogonal difference of L and M , i.e. $L \ominus M = L \cap (L \cap M)^\perp$

π_L Orthogonal projection onto L . Recall that if $a_1, \dots, a_d$ is an orthogonal basis of L , then $\pi_L x = \sum_{i=1}^d \frac{\langle x, a_i \rangle}{\|a_i\|^2} a_i$

π_ω Orthogonal projection onto $\text{span}\{\omega\}, \omega \in R^n$

Matrices

I_n	$n \times n$ identity matrix
$\det(A)$	Determinant of the matrix A
A^T	Transposed matrix of A
$SO(n)$	The group of rotations in R^n , special orthogonal transformations
$SO(n, L_r)$	The subgroup of $SO(n)$ consisting of rotations, keeping the r -subspace L_r fixed

Set operations

$X + y$	$= X + \{y\}, X \subseteq R^n, y \in R^n$
$\check{X}$	$= \{-x : x \in X\}, X \subseteq R^n$
$X \setminus Y$	Set difference, $= \{z \in R^n : z \in X, z \notin Y\}, X, Y \subseteq R^n$
$\text{diam} X$	$= \sup\{\ x - x'\ : x \in X, x' \in X\}, X \subseteq R^n$
$\text{conv} X$	Convex hull, the smallest convex set containing $X \subseteq R^n$
∂X	Boundary of $X \subseteq R^n$
$\text{star} X$	The part of $X \subseteq R^n$ which can be seen directly from O , $= \{x \in X : [O, x] \subseteq X\}$

Measures

$\mathcal{B}^n$	The Borel σ -algebra in R^n
$\mathcal{B}_0^n$	The set of bounded Borel sets
$\mathcal{A} \otimes \mathcal{B}$	The product of the σ -algebras $\mathcal{A}$ and $\mathcal{B}$
μ_T $(\mu)_T$	The measure μ lifted by the mapping T , i.e. $\mu_T(A) = \mu(T^{-1}(A))$
λ_n^d	d -dimensional Hausdorff measure in R^n
dx^d	$= \lambda_n^d(dx)$
λ_n	Lebesgue measure in $R^n, = \lambda_n^n$
V	Volume in R^3 or generally in R^n , Lebesgue measure
S	Surface area in R^3 or $R^n, = \lambda_n^{n-1}$
L	Length in R^2, R^3 or $R^n, = \lambda_n^1$
$ \cdot $	Number of elements in $\cdot, = \lambda_n^0$

$\mu_{p(r)}^n$	Rotation invariant measure on $\mathcal{L}_{p(r)}^n$
$dL_{p(r)}^n$	$= \mu_{p(r)}^n(dL_p)$
$\nu_{p(r)}^n$	Rotation invariant measure on $\mathcal{T}_{p(r)}^n$
$dT_{p(r)}^n$	$= \nu_{p(r)}^n(dT_p)$
η_q^n	Measure on $\mathcal{G}_q^n$, invariant under rotations and translations
dG_q^n	$= \eta_q^n(dG_q)$

Functions

g_i or $(g)_i$	The i 'th coordinate function of $g : R^n \rightarrow R^k$
$g \equiv c$	The function g is constant equal to c
$\ker g$	The kernel of $g : R^n \rightarrow R^k$, i.e. $\ker g = g^{-1}(O)$
$\mathbf{1}\{\cdot\}$	Indicator function
$[\cdot]$	Integer part
$\Gamma(\cdot)$	The gamma function
$B(\cdot, \cdot)$	The Beta function
$F(\cdot, \cdot, \cdot; \cdot)$	The hypergeometric function
$P_k(\cdot)$	The k 'th Bernoulli polynomial, $k = 0, 1, \dots$
∇_p	$\nabla_p(x_1, \dots, x_p) = p! \lambda_n^p(\text{conv}\{O, x_1, \dots, x_p\})$

Differential calculus

$Df(x)$	$k \times n$ matrix of partial derivatives of the differentiable function $f : R^n \rightarrow R^k$ at $x \in R^n$
$f'(x)$	$= Df(x)$ for $n = k = 1$
$\text{Tan}[X, x]$	Tangent space of X at $x \in X$
$Jf(x; X)$	Generalized Jacobian

Statistics

$E(X)$	Mean of the random variable X
$\text{Var}(X)$	Variance of the random variable X
$\text{Cov}(X, Y)$	Covariance between the two random variables X and Y
$N(\mu, \sigma^2)$	The normal distribution on R with mean μ and variance σ^2

$b(n, p)$	The binomial distribution with number parameter n and probability parameter p
$\chi^2(f)$	The χ^2 -distribution with f degrees of freedom
$B(\alpha, \beta)$	The Beta distribution with parameters α and β
$\sim$	The notation $X \sim b(n, p)$ is used in the case where the random variable X is binomial distributed, say
$F_{a,b}$	Distribution function of the Beta distribution with parameters $(a/2, b/2)$
$h_{p(r)}^{(n)}$	The quantity $h_{p(r)}^{(n)}(x, L_r)$ is the probability that $x \in R^n$ belongs to an isotropic p -slice of thickness $2t$, containing L_r
a.s.	Almost surely convergence
$\xrightarrow{\sim}$	Convergence in distribution
$o(\cdot)$	Small o function, $f = o(g)$ if $f/g \rightarrow 0$ in some limit
$O(\cdot)$	Big O function, $f = O(g)$ if f/g is bounded in some limit