Characterization of mammary gland tissue

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Overview

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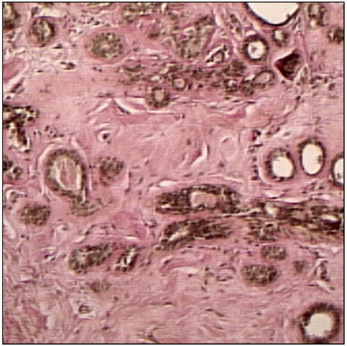
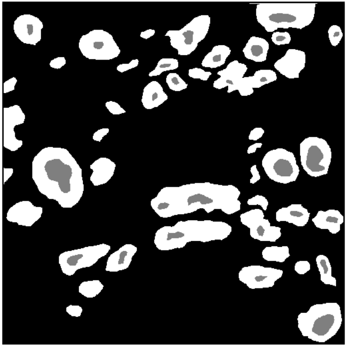


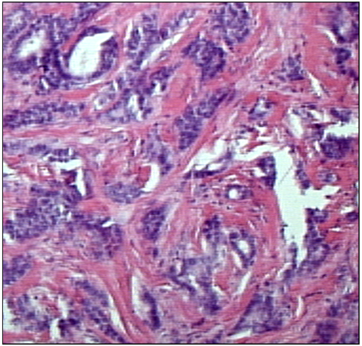
(a) Original microscopic image



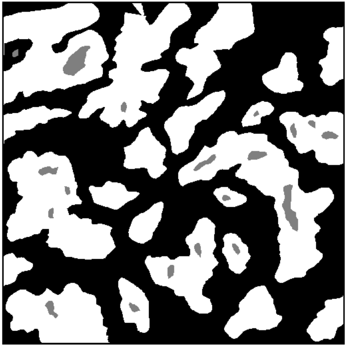
(b) Partitioned image

Figure: Carcinoma-free mammary gland tissue, 10-times magnified

1 Introduction



(a) Original microscopic image



(b) Partitioned image

Figure: Mammary carcinoma tissue, 10-times magnified

1 Introduction

- Characterization of the morphological structure of these images by the specific intrinsic volumes.
- Estimation of the specific intrinsic volumes.
- Estimation of the asymptotic variances of the specific intrinsic volumes.
- Test if an image shows carcinoma-free tissue or not.

Overview

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2. Estimation of the specific intrinsic volumes
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2.1 Estimation of the specific intrinsic volumes

Let Ξ be a stationary germ-grain model.
For any $x \in \mathbb{R}^d$ and any positive radius r it holds that

$$\mathbb{E} V_0 \left(\Xi \cap B_r(x)\right) = \sum_{j=0}^{d} r^{d-j} \kappa_{d-j} \overline{V}_j(\Xi),$$

where $\overline{V}_j(\Xi)$, $j = 0, \ldots, d$ denote the specific intrinsic volumes.

For $d = 2$ these are

- $\overline{V}_0 =$ number of clumps - number of holes per unit area,
- $\overline{V}_1 = 1/2$ boundary length per unit area,
- $\overline{V}_2 =$ area fraction.

With $d+1$ positive, pairwise different radii $0 < r_0 < \ldots < r_d$ we get the following system of linear equations

$$\begin{pmatrix} r_0^d k_d & \cdots & r_0 k_1 & 1 \\ r_1^d k_d & \cdots & r_1 k_1 & 1 \\ \vdots & \ddots & \vdots & \vdots \\ r_d^d k_d & \cdots & r_d k_1 & 1 \end{pmatrix} \begin{pmatrix} \overline{V}_0(\Xi) \\ \vdots \\ \overline{V}_d(\Xi) \end{pmatrix} = \begin{pmatrix} \mathbb{E} V_0(\Xi \cap B_{r_0}(o)) \\ \vdots \\ \mathbb{E} V_0(\Xi \cap B_{r_d}(o)) \end{pmatrix}$$

or in short

$$Av = y.$$

2.1 Estimation of the specific intrinsic volumes

With an estimator $\widehat{y}$ for y we can estimate v by

$$\widehat{v} = A^{-1}\widehat{y}.$$

To estimate the local Euler characteristic we define the stationary random field $Y(x) = V_0(\Xi \cap B_{r_i}(x))$.

Then an unbiased estimator for $\mathbb{E}V_0(\Xi \cap B_{r_i}(o))$ is given by

$$\widehat{y} = \frac{1}{|W \ominus B_{r_d}(o)|} \int\limits_{W \ominus B_{r_d}(o)} Y(x)\, dx.$$

2.2 Least-squares estimator

Let $0 < r_0 < \ldots < r_{k-1}$ be $k > d + 1$ pairwise different radii. The estimator

$$v^* = \left(A^\top A\right)^{-1} A^\top \widehat{y}$$

is the solution of the least-squares minimization problem

$$|\widehat{y} - Av^*| = \min_{x \in \mathbb{R}^{d+1}} |\widehat{y} - Ax|$$

and an estimator for $y = \left(\overline{V}_0(\Xi), \ldots, \overline{V}_d(\Xi)\right)^\top$.

2.2 Least-squares estimator

Under certain conditions it holds that

$$\sqrt{|W_n|}\left(v_2^* - \overline{V}_2(\Xi)\right) \xrightarrow{d} \mathcal{N}\left(0, \sigma^2\right).$$

With an unbiased and consistent estimator $\widehat{\sigma}^2$ for σ^2 it holds that

$$\sqrt{|W_n|}\frac{v_2^* - \overline{V}_2(\Xi)}{\widehat{\sigma}} \xrightarrow{d} \mathcal{N}(0, 1),$$

where $\{W_n\}$ is an sequence of unboundedly increasing observation windows.

In practice the images should be as big as possible!

2.3 Step by step

1. Choose the radii $r_i = 4.2 + 1.3i, \quad i = 0, \ldots, 14.$

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2. Estimate the local Euler characteristic in $W \ominus B_{r_{14}}(o)$ for all radii $r_0, \ldots, r_{14}$ by computing $V_0 (\Xi \cap B_{r_i}(x))$ for all pixels $x \in W \ominus B r_{14}(o)$ and averaging over all pixels.

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3. Estimate the specific intrinsic volumes by computing the least-squares estimator v^*.

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3. Estimate the specific intrinsic volumes by computing the least-squares estimator v^*.

4. Choose the averaging set $U = B_{300}(o)$ and estimate the covariance $\mathrm{Cov}_Y(x)$ of the random field Y for all pixels $x \in U$.

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1. Choose the radii $r_i = 4.2 + 1.3i, \quad i = 0, \ldots, 14.$
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3. Estimate the specific intrinsic volumes by computing the least-squares estimator v^*.
4. Choose the averaging set $U = B_{300}(o)$ and estimate the covariance $\mathrm{Cov}_Y(x)$ of the random field Y for all pixels $x \in U$.
5. Estimate the variance σ^2 of $\sqrt{|W|}\left(v_2^* - \overline{V}_2(\Xi)\right)$.

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3. Estimate the specific intrinsic volumes by computing the least-squares estimator v^*.

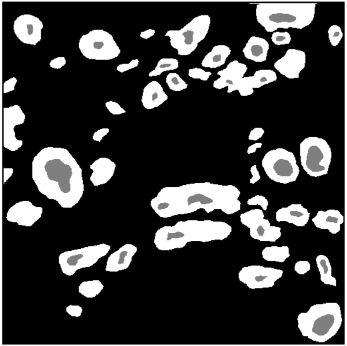
4. Choose the averaging set $U = B_{300}(o)$ and estimate the covariance $\mathrm{Cov}_Y(x)$ of the random field Y for all pixels $x \in U$.

5. Estimate the variance σ^2 of $\sqrt{|W|}\left(v_2^* - \overline{V}_2(\Xi)\right)$.

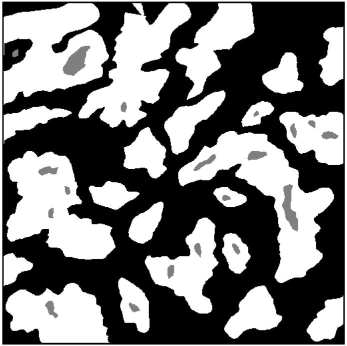
6. Then it holds that $\sqrt{|W|}\left(v_2^* - \overline{V}_2(\Xi)\right)/\widehat{\sigma}$ is approximately normally distributed.

Overview

3.1 Examples



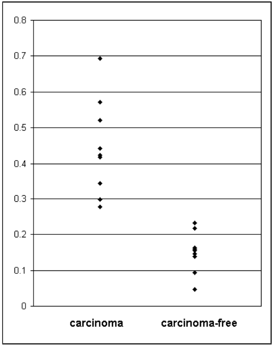
(a) Carcinoma-free tissue



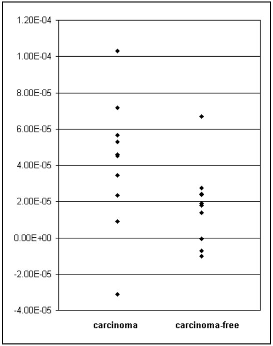
(b) Mammary carcinoma tissue

Figure: Carcinoma-free tissue vs. mammary carcinoma tissue

3.1 Examples



(a) Area fraction white phase



(b) Euler characteristic white phase per unit area

Figure: Examples for the specific intrinsic volumes of the two groups

3.2 Statistical test on carcinoma-free tissue

Null hypothesis

$$H_0 : p_j = p_0$$

where

$p_j =$ expected area fraction of the white phase in image $j = 1, \ldots, 20$ and

$p_0 =$ mean area fraction of the white phase in images showing carcinoma-free tissue

vs. the alternative $H_1 : p_j > p_0$ with significance level $\alpha = 5\,\%$.

3.2 Statistical test on carcinoma-free tissue

By Slutsky's theorem the test statistic

$$T_j = \sqrt{|W|}\,\frac{\widehat{p}_j - p_0}{\widehat{\sigma}_j}$$

is approximately normally distributed, where

$\widehat{p}_j$ = least-squares estimator for the area fraction of the white phase in image j and

$\widehat{\sigma}_j^2$ = estimated variance of $\sqrt{|W|}\,(\widehat{p}_j - p_0)$.

3.2 Statistical test on carcinoma-free tissue

j	$\widehat{p}_j$	T_j	Rejection of H_0
1	0.047224	-5.758985	no
2	0.094392	-2.312868	no
3	0.138055	-3.038629	no
4	0.145576	-0.188148	no
5	0.155753	0.136175	no
6	0.159763	0.209195	no
7	0.163755	0.372340	no
8	0.163812	0.350634	no
9	0.217735	1.520662	no
10	0.232209	1.498260	no

Table: Results of the test $H_0 : p_j = p_0$ for images showing carcinoma-free tissue

3.2 Statistical test on carcinoma-free tissue

j	$\widehat{p}_j$	T_j	Rejection of H_0
11	0.277096	5.442611	yes
12	0.297491	5.157528	yes
13	0.342711	4.504925	yes
14	0.342963	2.149426	yes
15	0.418210	10.787309	yes
16	0.423122	5.853516	yes
17	0.442027	6.305909	yes
18	0.520348	10.887926	yes
19	0.570691	24.584655	yes
20	0.693262	7.609358	yes

Table: Results of the test $H_0 : p_j = p_0$ for images showing mammary carcinoma tissue

3.3 Statistical test on mammary carcinoma tissue

Null hypothesis

$$H_0 : p_j = p_0$$

vs. the alternative $H_1 : p_j < p_0$ with significance level $\alpha = 5\,\%$, where

$p_0 =$ mean area fraction of the white phase in images showing mammary carcinoma tissue.

By Slutsky's theorem the test statistic

$$T_j = \sqrt{|W|}\,\frac{\widehat{p}_j - p_0}{\widehat{\sigma}_j}$$

is approximately normally distributed.

3.3 Statistical test on mammary carcinoma tissue

j	$\widehat{p}_j$	T_j	Rejection of H_0
1	0.047224	-19.104942	yes
2	0.094392	-12.264340	yes
3	0.138055	-58.523974	yes
4	0.145576	-7.780054	yes
5	0.155753	-8.648982	yes
6	0.159763	-6.477981	yes
7	0.163755	-7.558520	yes
8	0.163812	-7.082725	yes
9	0.217735	-4.465708	yes
10	0.232209	-3.364893	yes

Table: Results of the test $H_0 : p_j = p_0$ for images showing carcinoma-free tissue

j	$\widehat{p}_j$	T_j	Rejection of H_0
11	0.277096	-7.516248	yes
12	0.297491	-5.322946	yes
13	0.342711	-2.362169	yes
14	0.342963	-1.122410	no
15	0.418210	-0.656133	no
16	0.423122	-0.231814	no
17	0.442027	0.222966	no
18	0.520348	2.874257	no
19	0.570691	8.993118	no
20	0.693262	4.067400	no

Table: Results of the test $H_0 : p_j = p_0$ for images showing mammary carcinoma tissue

Overview

4 Conclusion

- Estimation of the vector of specific intrinsic volumes (theory and algorithmic implementation exist).
- Estimation of the specific intrinsic volumes and their asymptotic covariance matrix from one single image.
- Better results when testing on carcinoma-free tissue.
- Estimation of the variance by dividing the image into sub-images and calculating the sample variance yields worse results.

Overview

5 References

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