
# Application of Shape Analysis on renal tumors

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# Outline

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Every object $o_i$ in a space $V$ of dimension $m$ is thus represented in a space of dimension $k \cdot m$ by a set of landmarks:

$$\forall i = 1 \dots n,\ o_i = \{l_1 \dots l_k\}, l_j \in \mathbb{R}^m. \tag{1}$$

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1. For every $i, i = 1, ..., n$, the size of each object is determined as the euclidian norm of their landmarks.

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2. The landmarks are standardized by dividing them by the size of their object:

$$\tilde{l}_j^i = \frac{l_j^i}{\|o_i\|}. \tag{3}$$

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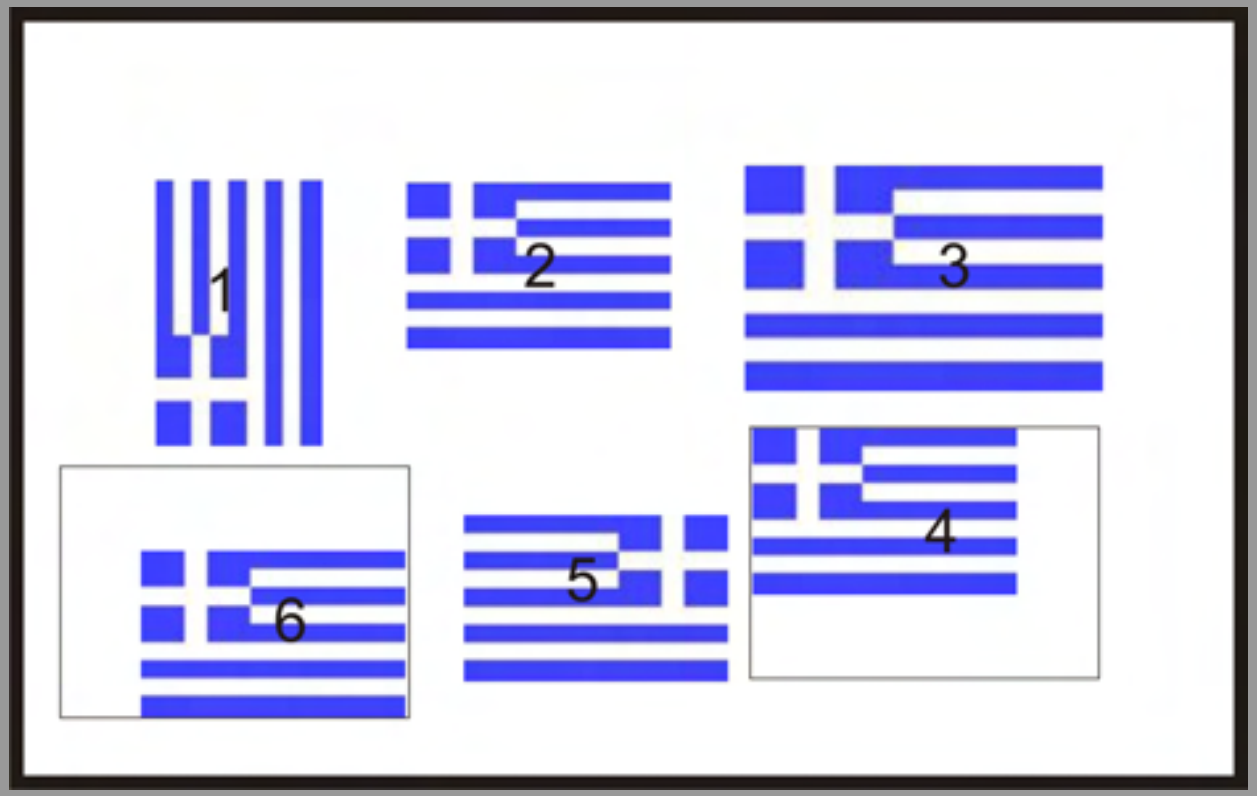
2. We center all the landmarks by subtracting this mean:

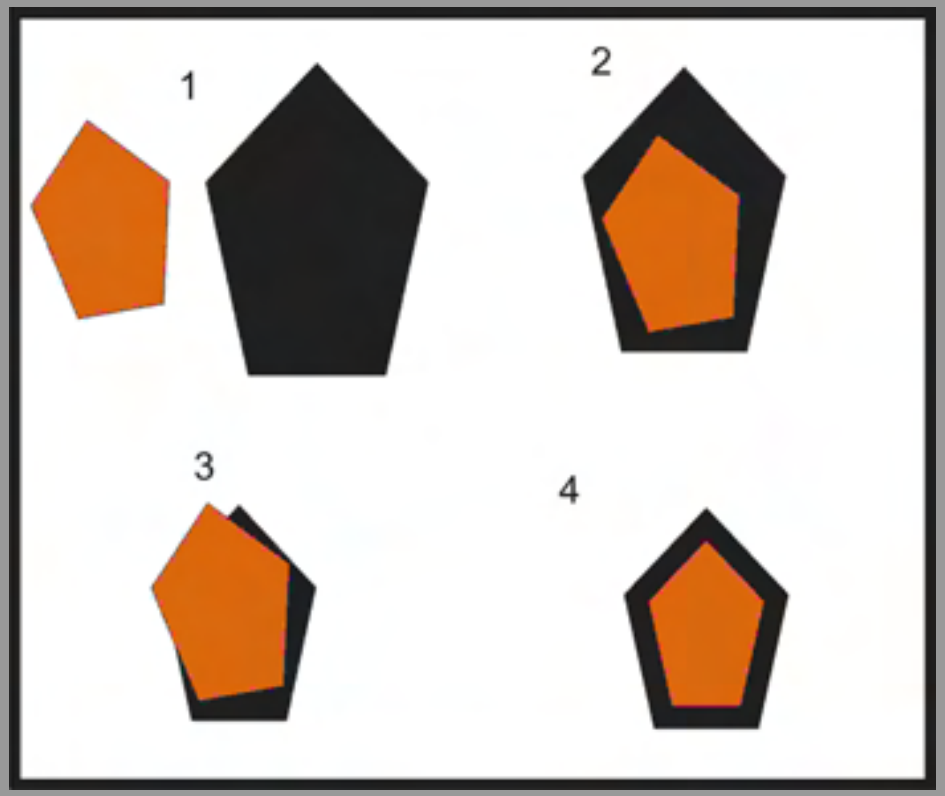
$$\bar{l}_j^i = l_j^i - z^i \tag{5}$$

# Removing the location/scale




location (4,6), scale (3), rotation (1) and reflection (3)

# Removing the location/scale




Mathematical procedure for removing location/scale two objects

# Remark for application

We do not need to remove rotation in our application "medicine", since we use MRI images of the tumors which are frontal or transversal images.
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Hence, we are able to work completely in the standard three-dimensional space with the euclidian norm.

We do not need any further procrustes analysis nor any complicated stochastic geometry. It is easy to show that the partial procrustean distance is the euclidean distance after transformation.

# The mean shape

To compare the standardized and centered sets of landmarks, we need to define the mean shape of all the objects and a distance function which allows us to evaluate how "near" every object is from this mean shape.

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If $X$ denotes a random variable defined on a probability space $(\Omega, \mathcal{F}, \mathcal{P})$ with values in a metric space $(\Xi, d)$, an element $m \in \Xi$ is called a mean of $x_1, x_2, ..., x_k \in \Xi$ if

$$\sum_{j=1}^{k} d(x_j, m)^2 = \inf_{\alpha \in \Xi} \sum_{j=1}^{k} d(x_j, \alpha)^2. \tag{6}$$

# The mean shape

That means that the mean shape is defined as the shape with the smallest variance of all shapes in a group of objects. Every distance is continuous ( Proof: using the triangle inequality for a metric and the $\epsilon - \delta$ criterion). So we are able to find values minimizing the variance. We have to look for the minimum with the smallest variance.

# The mean shape and the $L^p$-norm

The mean shape in a finite dimensional space. Not considering the rotation we are searching for the minimum $m$ of:

$$f(m) = ||x - m||_p^2 \tag{7}$$

Differentiation with respect to m:

$$f'(m) = 2(-p\sum_{i=1}^{n}(m - x_i)^{-1+p}\sum_{i=1}^{n}(m - x_i)^p)^{-1+\frac{2}{p}}) \tag{8}$$

Now we have to solve for $m$.

$$0 = 2(-p\sum_{i=1}^{n}(m - x_i)^{-1+p}\sum_{i=1}^{n}(m - x_i)^p)^{-1+\frac{2}{p}}) \tag{9}$$

It is easy for $p = 1$ and $p = 2$.

# The mean shape and the $L^p$-norm

For $p = 1$ we take $|x_i| = \sqrt{(x_i)^2}$

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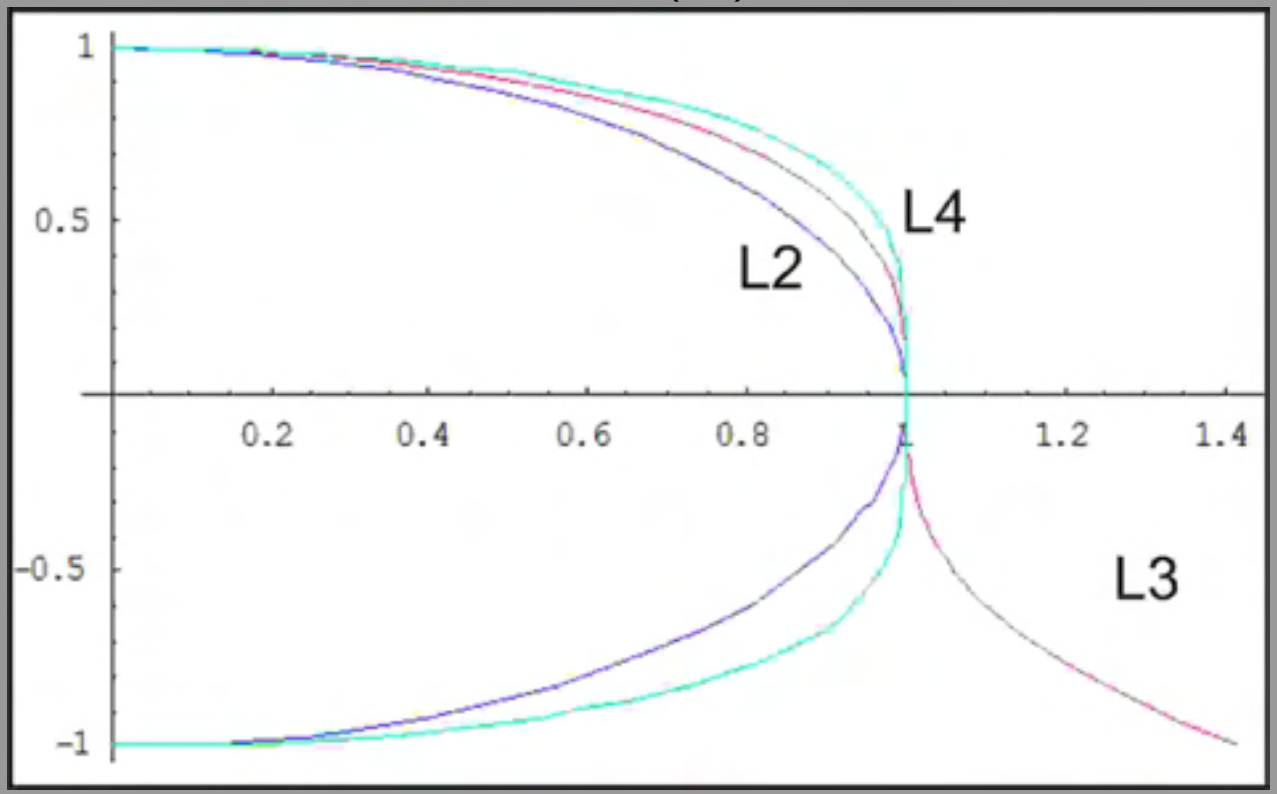
For $p = 3$ we get:

$$m = \frac{1}{2n} \sum_{i=1}^{n} 2x_i \pm \sqrt{(\sum_{i=1}^{n} 2x_i)^2 - 20(\sum_{i=1}^{n} x_i)} \tag{12}$$

# The mean shape and the $L^p$-norm

To show that $\frac{1}{2n}\sum_{i=1}^{n} 2x_i - \sqrt{(\sum_{i=1}^{n} 2x_i)^2 - 20(\sum_{i=1}^{n} x_i)}$ is a minimum, you put the result in $f''(m)$.



# The algorithm of Ziezold (1994)

The algorithm of Ziezold considering also the rotation of the objects for computing the mean shape. To begin, we fix the mean of all the standardized and centered objects as starting value:

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We then undertake the following steps for $i = 1, \ldots, n$

# The algorithm of Ziezold (1994)

1. $$\tilde{m} \mapsto w_i(\tilde{m}) = \begin{cases} \frac{\langle \tilde{m}, o_i \rangle}{|\langle \tilde{m}, o_i \rangle|} & \text{if } \langle \tilde{m}, o_i \rangle \neq 0 \\ 1 & \text{if } \langle \tilde{m}, o_i \rangle = 0 \end{cases} \tag{13}$$

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The stopping rule is $\tilde{m} = T(\tilde{m})$.

# Alternative: Elements of neural networks

Neural networks have been developed originally in order to understand the cognitive processes. A neuron perceives chemical and physical excitement from the environment by its dendrites. The neuron is processing this incoming data and sending the information to other neurons via axons and synapses. McCulloch and Pitts implemented the biological processes of a nerve cell for the first time in a mathematical way.
Nerve cells have to access and process incoming data in order to evaluate target information. Therefore the corresponding neural networks are called supervised neural networks.
An unsupervised neural network has no target and is similar to a cluster algorithm.

# Mathematical idea of neural networks

The data consist of $n$ variables $x_1, \ldots, x_n$ on binary scale. For data processing, the $i$th variable $x_i$ is weighted with $w_i$. Normalised with $|w_i| \leq 1$, multiplication of $x_i$ with $w_i$ determines the relevance of $x_i$ for a target $y$. The value $w_i$ reflects the correlation between the input variable and the target, the sign indicating the direction of the influence of the input variable on the target. Weighting the input variables for a target variable is similar to discriminant analysis.The critical quantity for the neuron is the weighted sum of input variables

$$q := \sum_{i=1}^{n} w_i \cdot x_i = w_1 \cdot x_1 + \ldots + w_n \cdot x_n \quad . \tag{16}$$

For a target $y$ with binary scale, a threshold $S$ is needed. Crossing the threshold yields 1 and falling below the threshold yields 0.

# Activation function

Hence the activation function $F$ can be written as

$$F(q) = \begin{cases} 1, & \text{if } x > S \\ 0, & \text{if } x \leq S \end{cases} \tag{17}$$

With the input of the activation function, we obtain $y = F(q)$ as

$$y = 1, \quad \text{if } \sum_{i=1}^{n} w_i \cdot x_i > S$$

$$y = 0, \quad \text{if } \sum_{i=1}^{n} w_i \cdot x_i \leq S$$

# Multi-layer perceptrons

In general a given target may be reached only up to a certain error. Given a certain measure $E(\widetilde{y}, y)$ for the distance between the given target state $y$ and the state $\tilde{y}$ computed by the neural network, the learning of the neural network corresponds to the minimisation of $E(\tilde{y}, y)$. The following training algorithm is inspired by Rumelhart, Hinton and Williams. The total error measure over all states of a given layer is defined as

$$E_{total}(\tilde{y}, y) := \frac{1}{2} \sum_{k=1}^{N} (\tilde{y}_k - y_k)^2 \quad . \tag{18}$$

It will be used below to reset the weights in each layer of the neural network.

# Mathematical procedure in detail

The processed state $\tilde{y}$ of the neural network is computed by the following steps. First the critical parameter for the first layer is computed from $n$ weighted input values as $\sum_{i=1}^{n} w_i \cdot x_i$. We consider a hidden output layer with $m$ neurons. For $j = 1, \ldots, m$, let $g_j$ be the activation function of the $j$-th neuron of the hidden layer, with an activation value of $h_j$, given as

$$h_j = g_j(\sum_{i=1}^{n} w_i \cdot x_i) \quad . \tag{19}$$

Usually for all neurons of a given layer a common activation function $g = g_1, \ldots, g_m$, e.g. a sigmoid function, is used.

Next, the output of the previous (hidden) layer becomes the input of the next layer, and the activation proceeds analogously to the previous layer. Let $f$ be the activation function of the pre-final (here the second) output layer. Then the pre-final critical value is

$$q = f(\sum_{j=1}^{m} u_j \cdot h_j) \quad . \tag{20}$$

Finally, the pre-final critical value $q$ is interpreted by a final activation function $F$ yielding

# Learning mechanism

The learning mechanism the weights is determined by the target distance measure

$$E = \frac{1}{2}\sum_{i=1}^{n}(y^i - \tilde{y}^i)^2 \quad .$$

The weights of both layers are changed according to the steepest descent, i.e.

$$\Delta w_i = \frac{\partial E}{\partial w_i} \tag{21}$$

$$\Delta u_j = \frac{\partial E}{\partial u_j} \tag{22}$$

# Learning mechanism

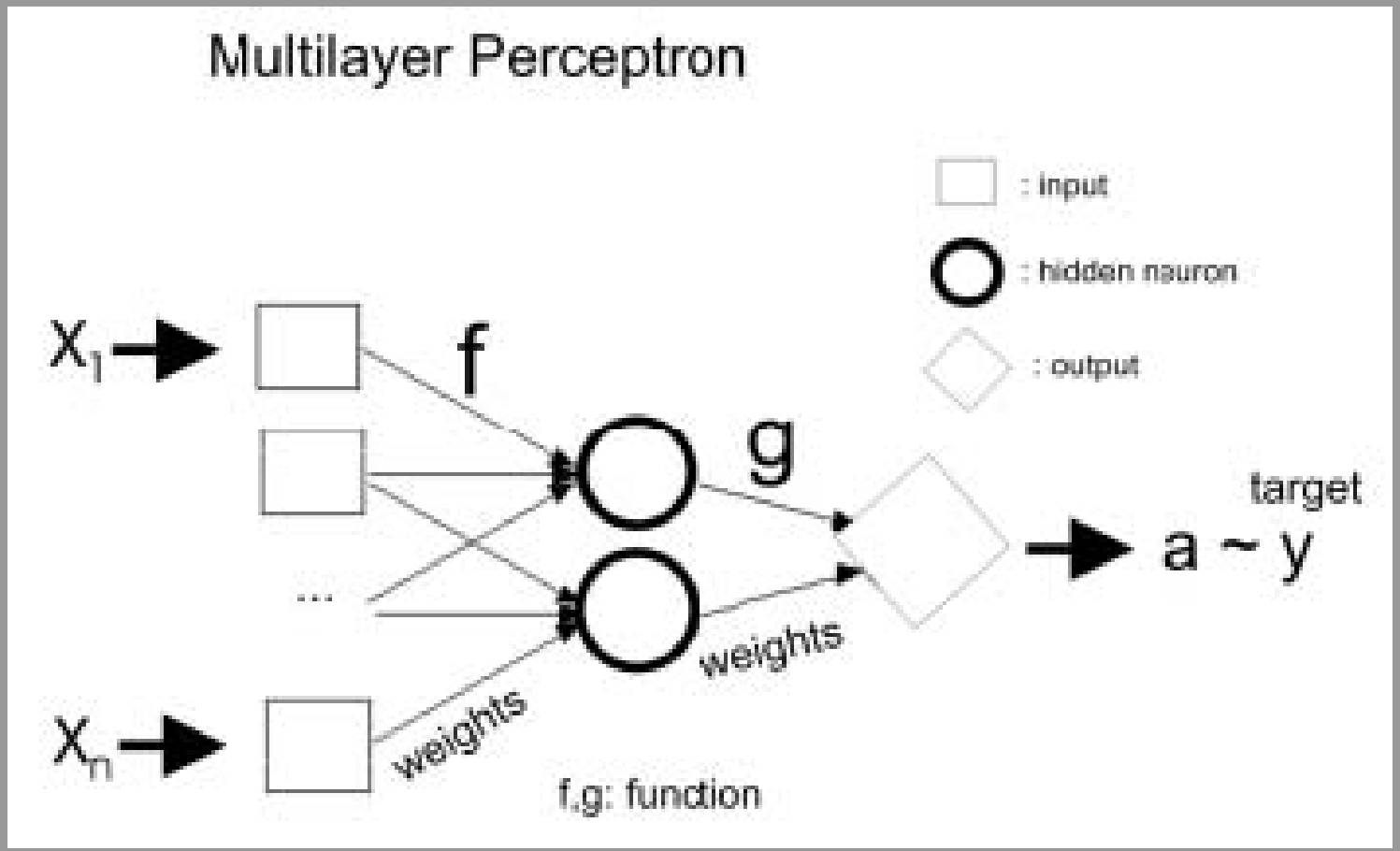
With a learning rate $\alpha$, which should be adapted to the data, the weights are changed as follows:

$$w_i^{new} = w_i^{old} - \alpha \cdot \Delta w_i \tag{23}$$

$$u_j^{new} = u_j^{old} - \alpha \cdot \Delta u_j \tag{24}$$

The necessary number of iterations depends on the requirements imposed by the data, the user, and the discipline.

# Learning mechanism



# Application on Shape Analysis

For simplicity, we consider now an 1-layer perceptron network, which is sufficient for our purpose of minimising the variance. Every landmark is weighted in every direction.

$$\sum_{j=1}^{k} d(x_j, m)^2 = \inf_{\alpha \in \Xi} \sum_{j=1}^{k} d(x_j, \alpha)^2. \tag{25}$$

In contrast to the former application of neural networks we are using a metric function instead of a binary variable. The difference between the weighted objects and the approximated mean shape is used instead of the difference between the reality and the approximation $E$.

# Application in medicine: Renal tumors in early childhood

- Nephroblastoma (Wilms-tumor) is the typical renal tumour in childhood. different types of histological tumor tissue (subtypes) exist, differentiated as a,b,c,d in our study. Three stages of risk and malignancy. Many renal tumors in the childhood are diagnosed as Wilms (130 per year).

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- Clearcell sarcoma is a renal high malignant tumour with possible bone metastases. Rare (12 per year).

# Application in medicine: Renal tumors in early childhood

In about 75% of patients MRI is used, otherwise CT is used (=different images, not comparable). Also we lost patients in consequence of quality.

# The data

Research sample:

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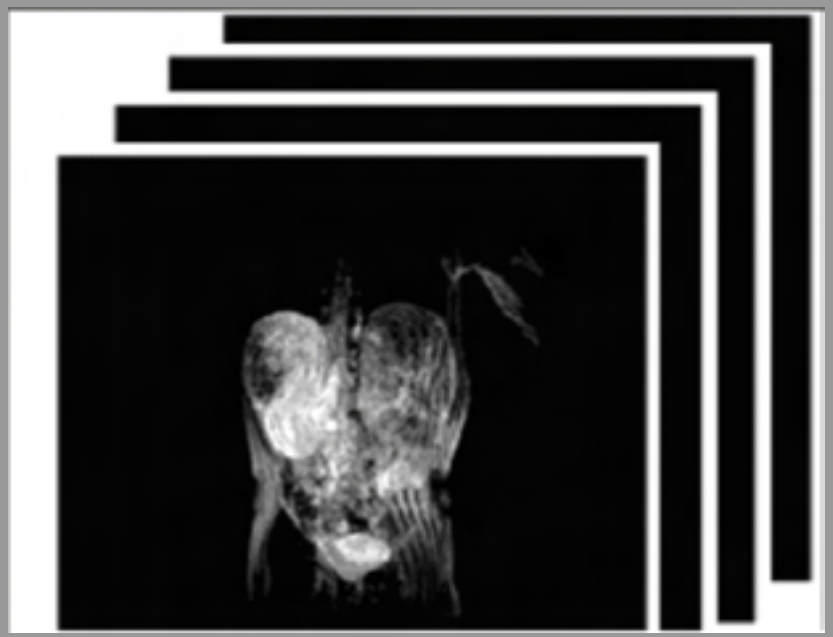
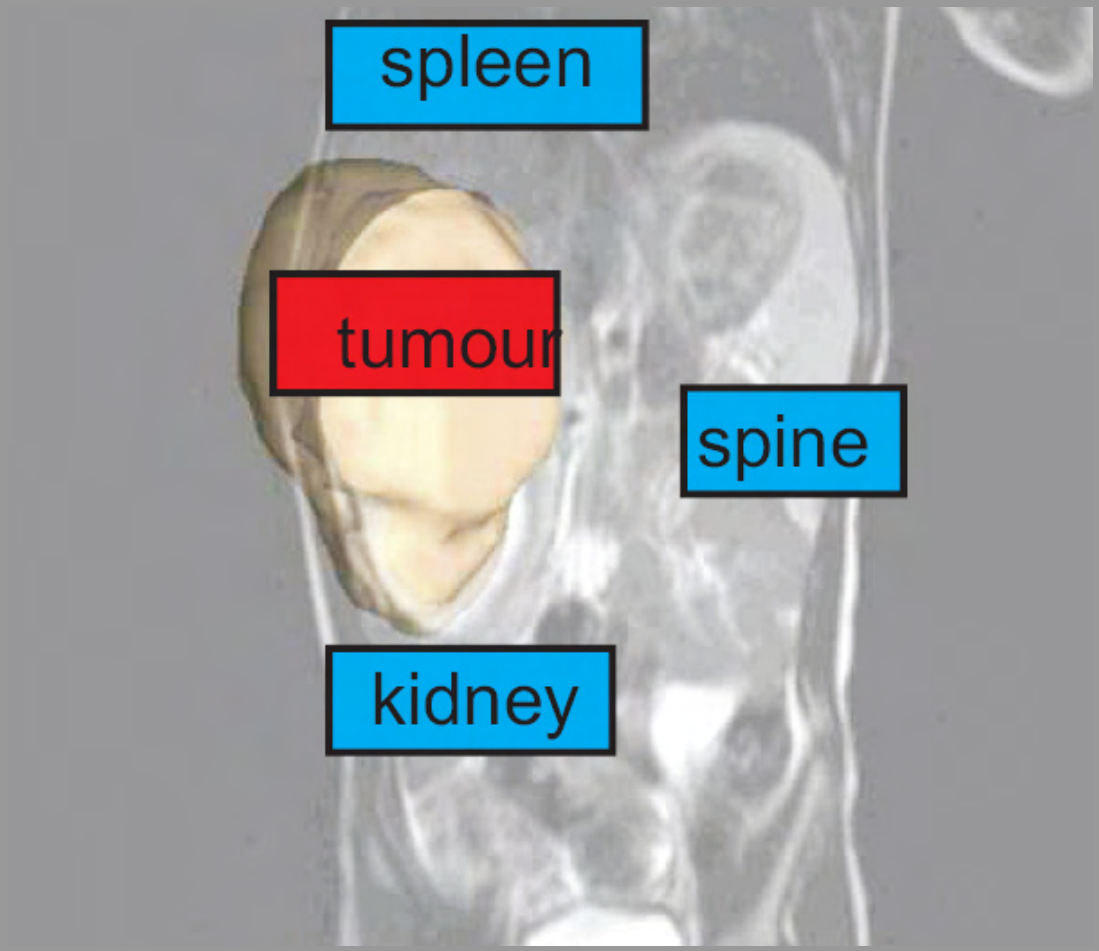


MRI image of a renal tumor in frontal view.

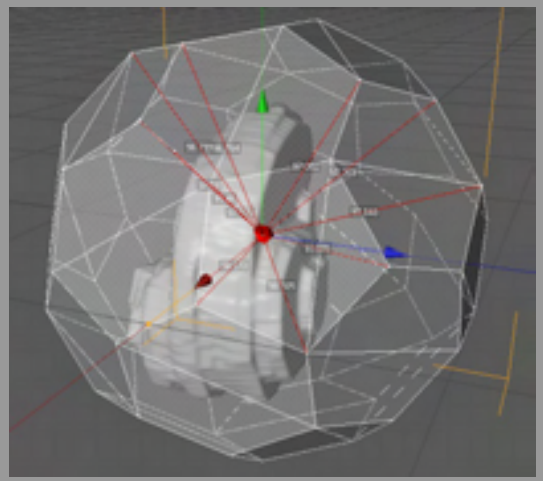
# The three-dimensional object




Three-dimensional model of a tumor.

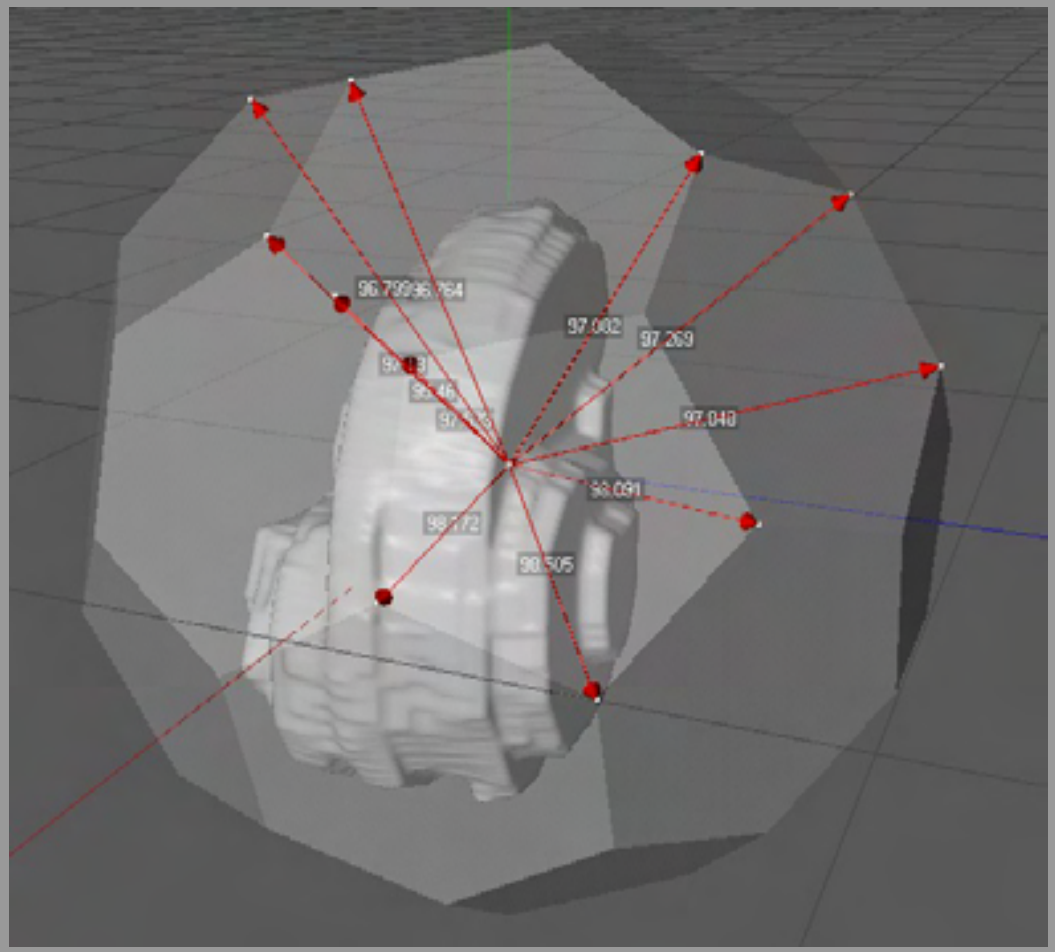
# Getting landmarks

To get $3D$ landmarks we construct a three dimensional object of the tumour from the $2D$ MRI. Then we take the intersection between the surface of the tumour and the vectors going from the centre to the edges of the platonic body C60 as landmarks as is shown in figure.



3D-Landmarks as cut points the edge of a platonic body / the surface of the tumor

# The platonic body C60




For every object, we consider the platonic body C60 whose center lies in the center of the object. This platonic body has 60 edges which give us 60 three-dimensional landmarks for every object.

# The landmarks

We take as landmarks the 60 points on the border of each object closest to the edges of the platonic body.

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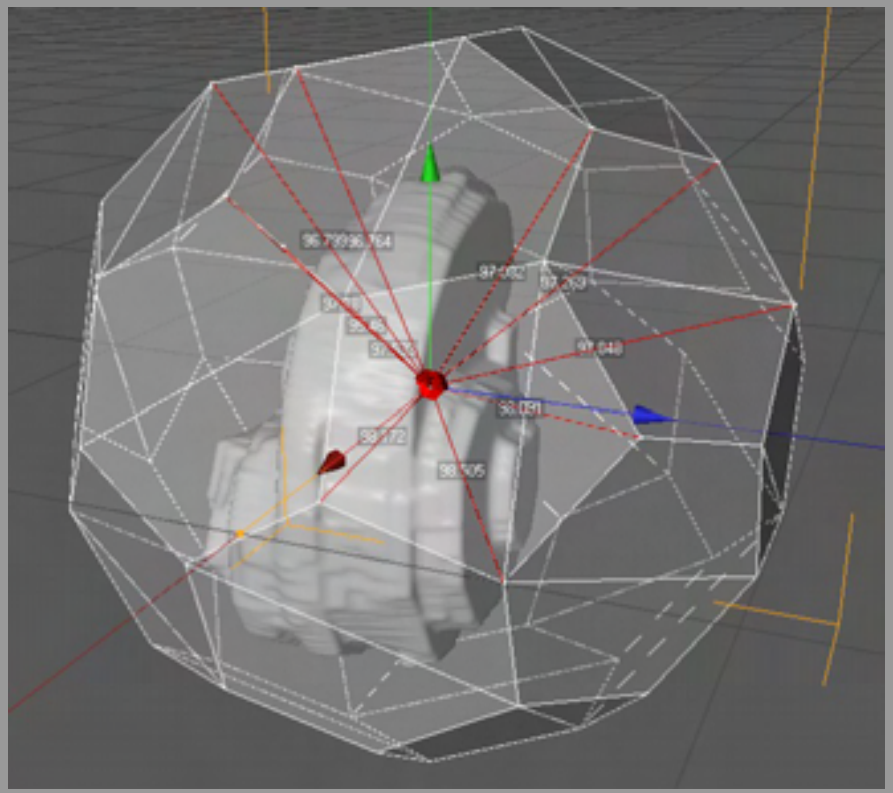
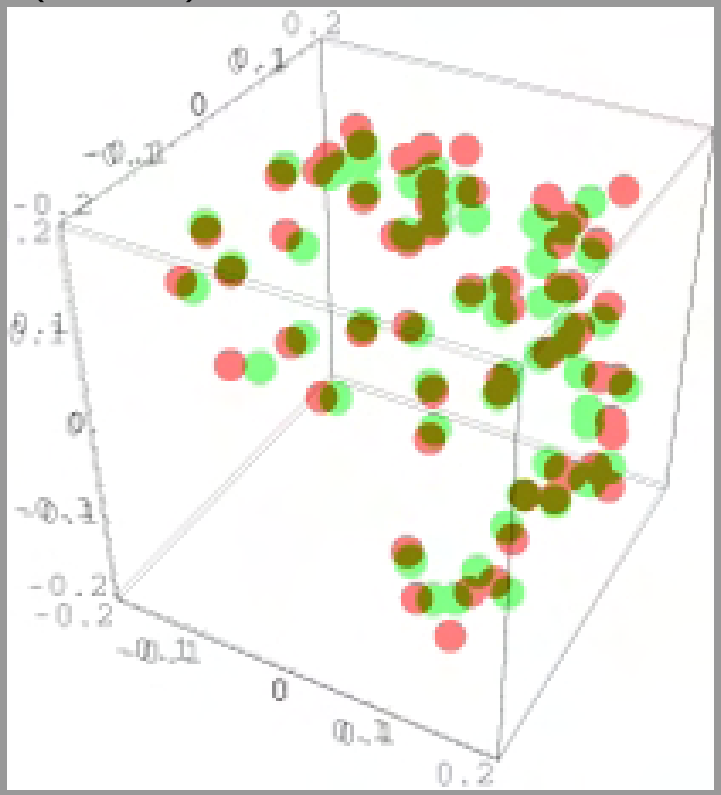


Only real measured points on the border of the tumor are taken, the approximated part of the three-dimensional object is not used.

# Examples of mean shapes

Figure shows the mean shape of the nephroblastomas (red) and of the neuroblastomas (green).




There are only 60 landmarks for describing a tumor

# Ziezold's test for differentiation of the types of tumors

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The subset $A$ is a realization of a distribution $P$ and the subset $B$ is an independent realization of a distribution $Q$.

The test hypotheses are:

$$\begin{aligned} \textit{Hypothesis:} \quad & H_0 : P = Q \\ \textit{Alternative:} \quad & H_1 : P \neq Q \end{aligned}$$

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3. Determination of all the possibilities of dividing the set into two subset with the same proportion.
4. Comparing the $u_0$-value to all possible $u$-values. Computing the rank (small u-value mean a small rank).
5. Calculate the $p$-value for $H_0$. $p_{r=i} = \frac{1}{\binom{N}{n}}$ for $i = 1, \ldots, \binom{N}{n}$, where $r$ is the rank for which we assume a uniform distribution.

# Mean variance of a set of shapes

We define the mean variance in the sense of Fréchet of a set of objects as the average of the distances to the mean shape.
If $X$ denotes a random variable defined on a probability space $(\Omega, \mathcal{F}, \mathcal{P})$ with values in a metric space $(\Xi, d)$ and $m \in \Xi$ is the mean of $x_1, x_2, ..., x_k \in \Xi$, $\sigma^2$ is the variance of $x_1, x_2, ..., x_k \in \Xi$ if

$$\sum_{j=1}^{k} d(d(x_j, m)^2, \sigma^2)^2 = \inf_{\alpha \in \Xi} \sum_{j=1}^{k} d(d(x_j, m)^2, \alpha)^2. \qquad (26)$$

That means that the variance is defined as the mean of the distances between the "mean shape" and the objects.

# The variance test

In this section we propose a test to compare the mean variance of two groups of objects. It functions analogously to the test of Ziezold (1994):

**step 1: Definition of the set of objects**

There is one set $M = \{o_1, \ldots, o_N\}$ that can be divided into two subsets: objects with the characteristics A: $A^{sample} = \{o_1, \ldots, o_n\} = \{a_1, \ldots, a_n\}$ and objects with the characteristics B: $B^{sample} = \{o_{n+1}, \ldots, o_N\} = \{b_1, \ldots, b_{N-n}\}$. The subset A is a realisation of a distribution $P$ and the subset B is an independent realisation of a distribution $Q$.

*Hypothesis:* $H_0 : \sigma_1^2 = \sigma_2^2$
*Alternative:* $H_1 : \sigma_1^2 \neq \sigma_2^2$
Define the *level of significance* $\alpha$. If the probability for $H_0$ is

# The variance test

**step 2: Computing the variance**

The variance is calculated by means of a straightforward generalisation of the algorithm of Ziezold (1994). Let $\sigma_1^2$ denote the variance of the subset $A$. $\sigma_2^2$ is then computed for the subset $B$.

**step 3: Computing the $F$-value**

$$F = \frac{|\hat{\sigma}_1^2|}{|\hat{\sigma}_2^2|}.$$

**step 4: Determination of all the possibilities of dividing the set into two subsets with given sizes**

**step 5: Comparing the $F$-value to all possible $F$-values. Computing the rank (small F-value mean a small rank).**

# The variance test

**step 6: Calculate the $p$-value for $H_0$**

$p_{r=i} = 1 - \frac{1}{\binom{N}{n}}$ for $i = 1, \ldots, \binom{N}{n}$, where $r$ is the rank for which we assume a rectangular distribution on the right side and $p_{r=i} = \frac{1}{\binom{N}{n}}$ on the left side.

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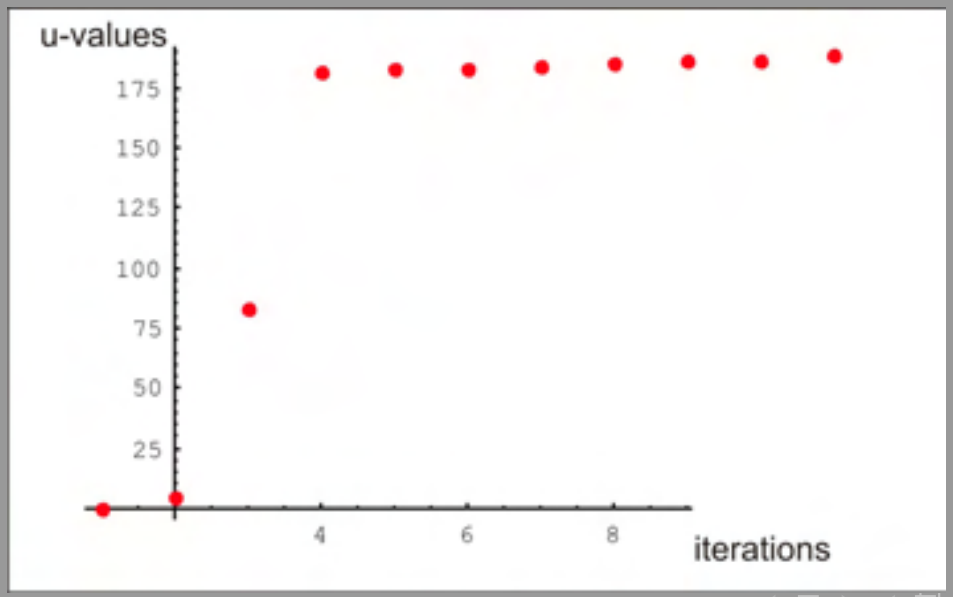
Wilms tumors are a homogeneous group.

# Results of variance test

The result of the test of Ziezold (1994) could be a consequence of different variances in the two groups. Our variance test allows to test this. For the renal tumours, the $F$-value for the differentiation of the variance of the group of nephroblastomas to the group of neuroblastomas is 1.28128 and the rank is 315. So the corresponding $p$-value is $1 - 0.315 = 0.685$ and we have to accept the null hyptothesis that the variance is similiar in both groups. So both kind of tumours seem to have more or less the same dispersion and a possible difference in the dispersion can be excluded as cause for difficulties in distinguishing the two kinds of tumours.

# Application of neural networks

Minimizing the variance in one of the groups does not lead always to an optimal differentiation between the different types of tumors. The neuronal network uses for minimizing the variance another metric. Every landmark is weighted in every direction. For a sample of 74 comparable tumors (69 nephroblastoma and 5 neuroblastoma the $u_0$-values are computed for the direction nephroblastoma vs. neuroblastoma.




u-values after every iteration of the MLP for minimizing the variance

# Conclusion

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# Outlook

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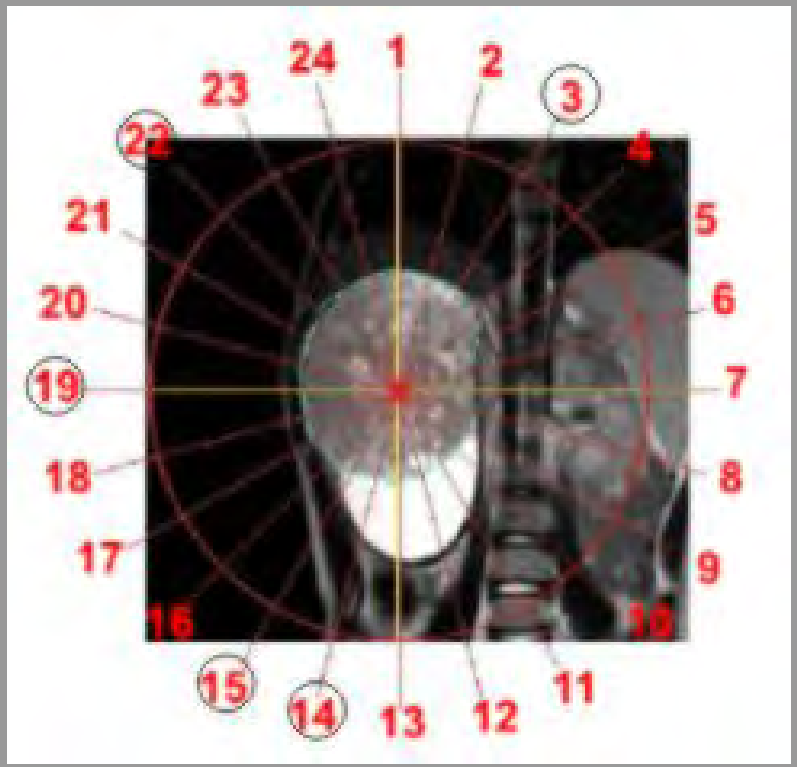
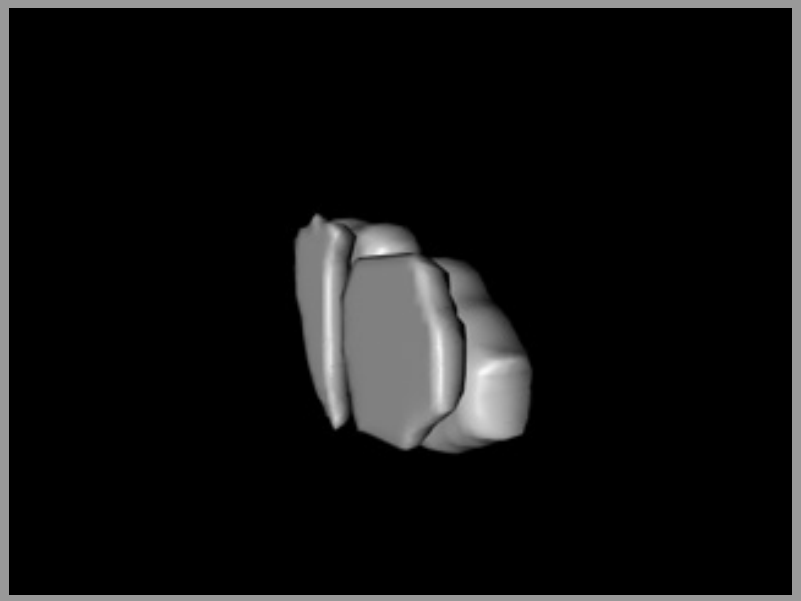
- Using the explorative procedure (Giebel 2007) for two and three dimensional landmarks. Aim: Find the relevant landmarks for differentiation.
- Including in the test the variance and other parameter. Estimating the difference by Tschebyscheff-formula.
- Dynamical Shape Analysis

# Outlook: Explorative procedure




Explorative procedure in 2D

# Outlook: Dynamical Shape Analysis

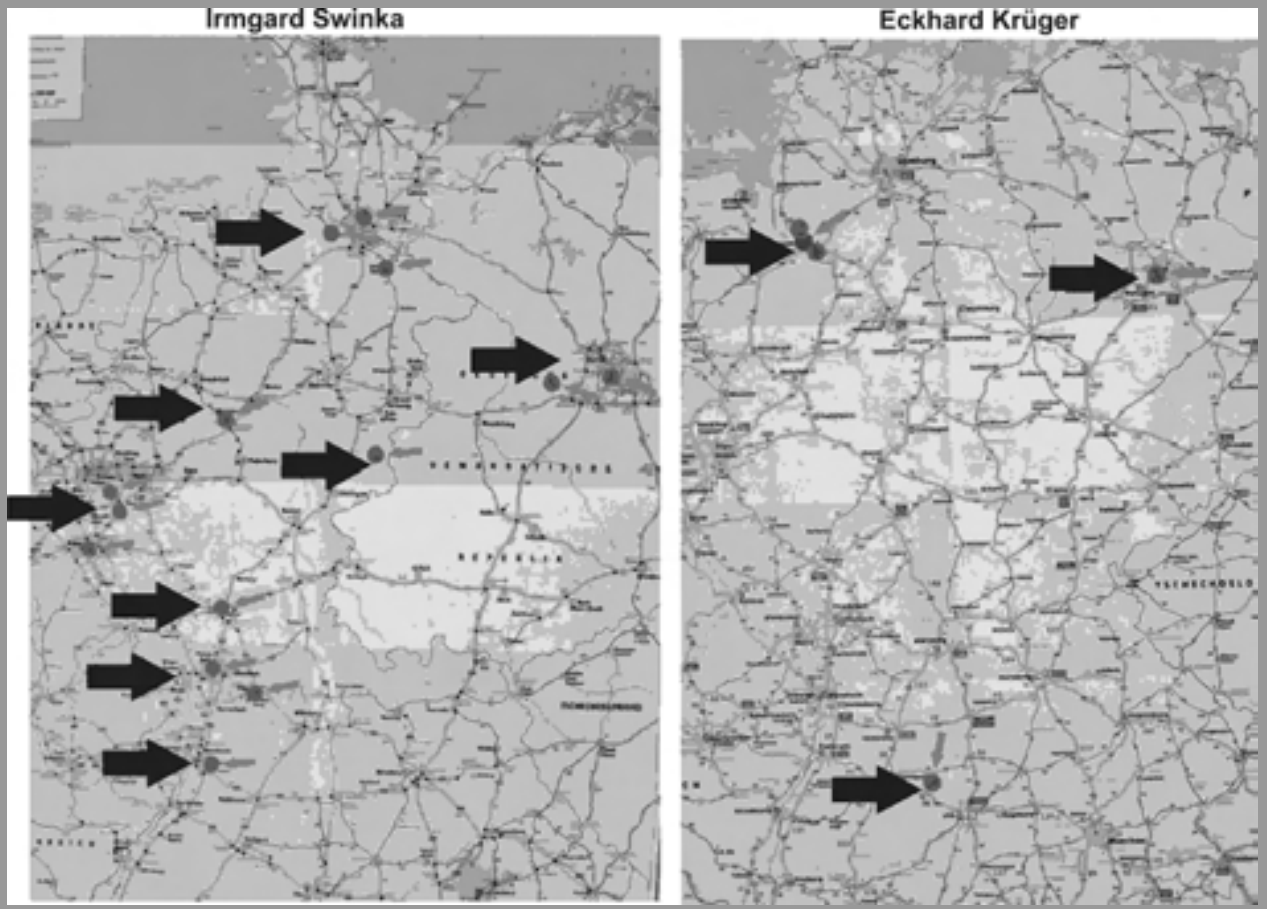


Diagnoses of hearts

Aim: Searching for a function between time point $t_1$ and $t_2$

# Outlook (Application field):

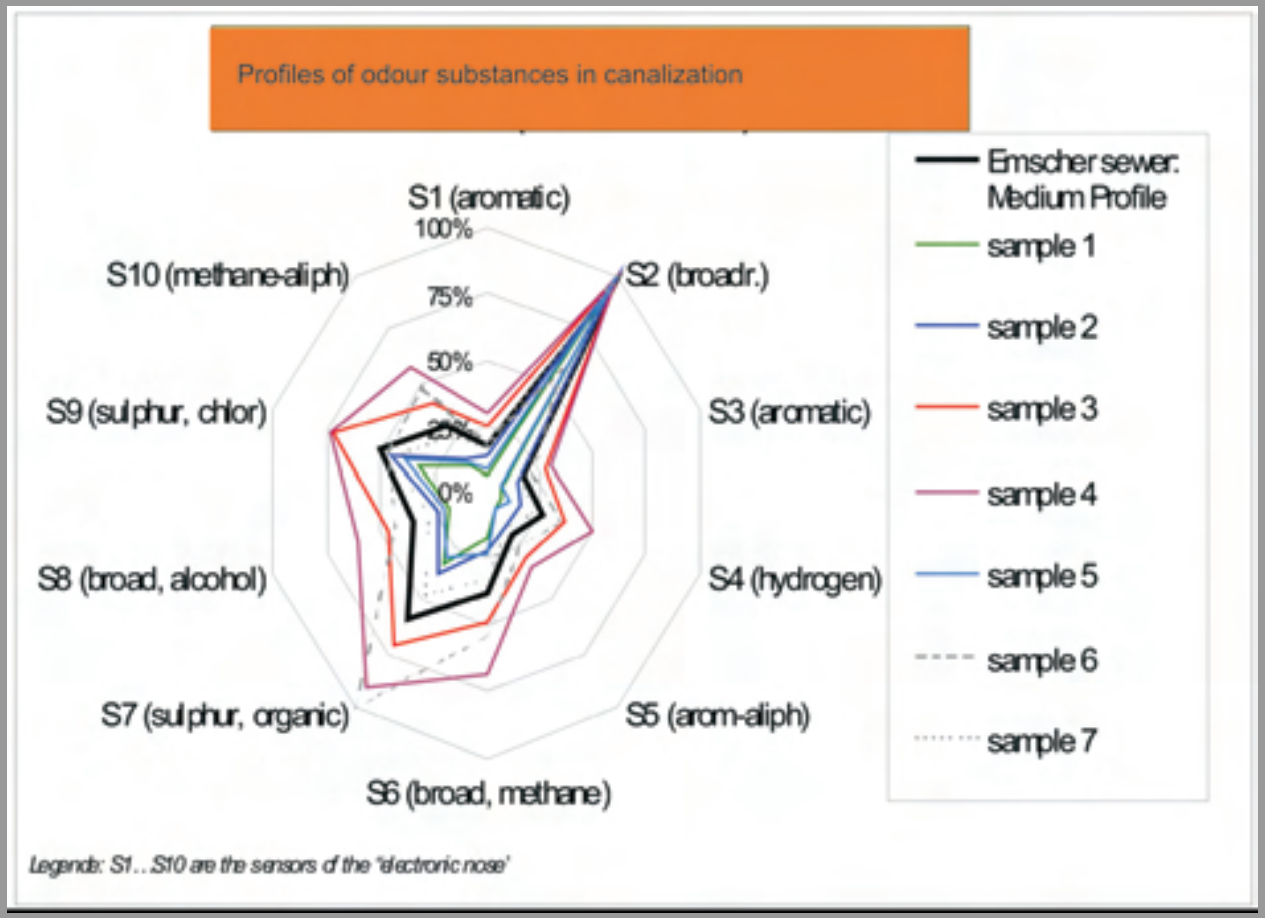
- Profiling criminals (offences in an ares)




The criminal has tu use the space with its structure. Comparing of objects with different landmarks is possible.

# Outlook (Application field):

- Application on electronic noses



# Thank you! Ba tashakor az tavajohe shama!

با تشکر از توجه شما