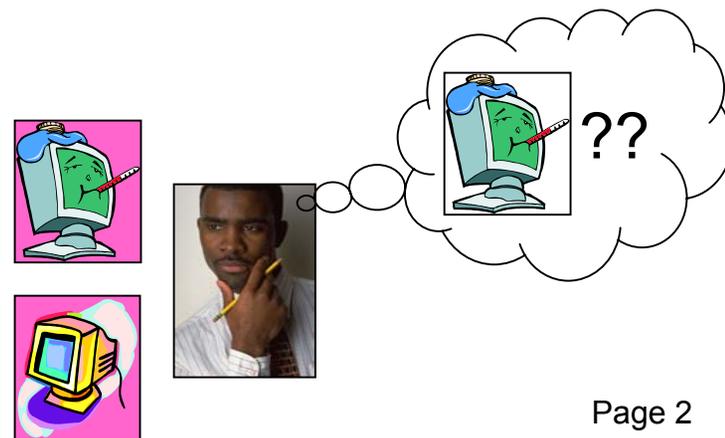
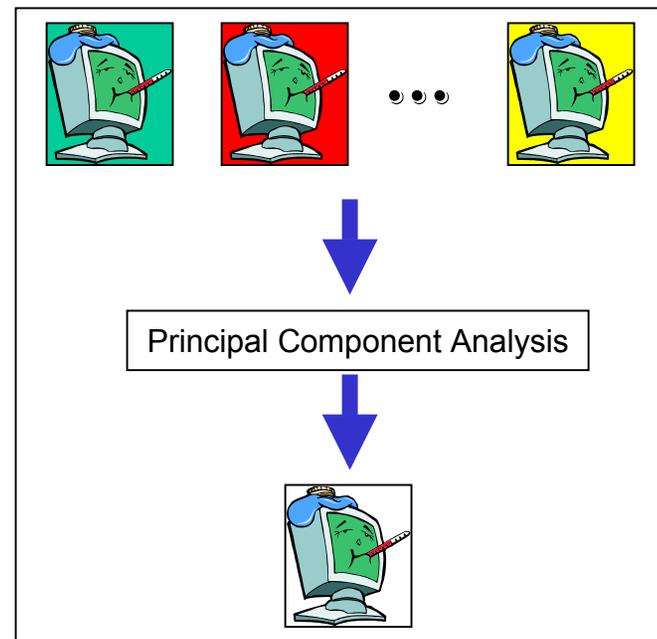


# Disease Detection Technique Using the Principal Orthogonal Decomposition on DNA Microarray Data

**David Peterson**  
**Dr. Charles H. Lee**

- Given a set of DNA microarray data from diseased samples
- Apply Principal Component Analysis (PCA) techniques to extract the primary component of the diseased samples (captures the diseased features)
- Perform simple disease detection tests by finding the projection of arbitrary samples onto the principal component



- We begin with a series of “snapshots”

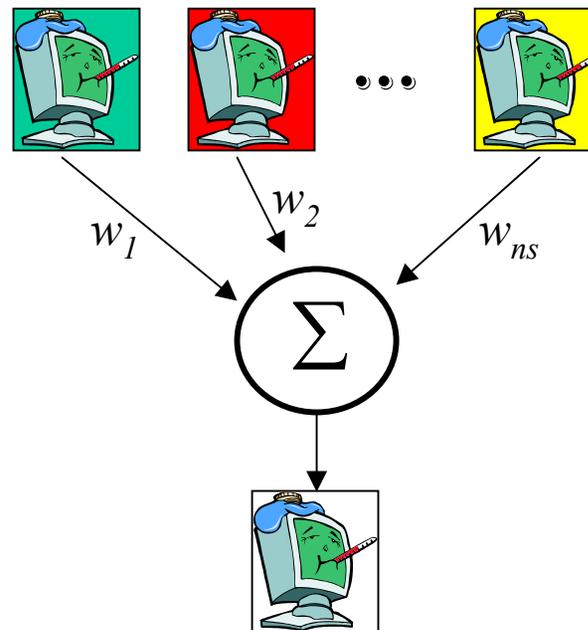
$$\{V_i(\vec{x})\}_{i=1}^{n_s}$$

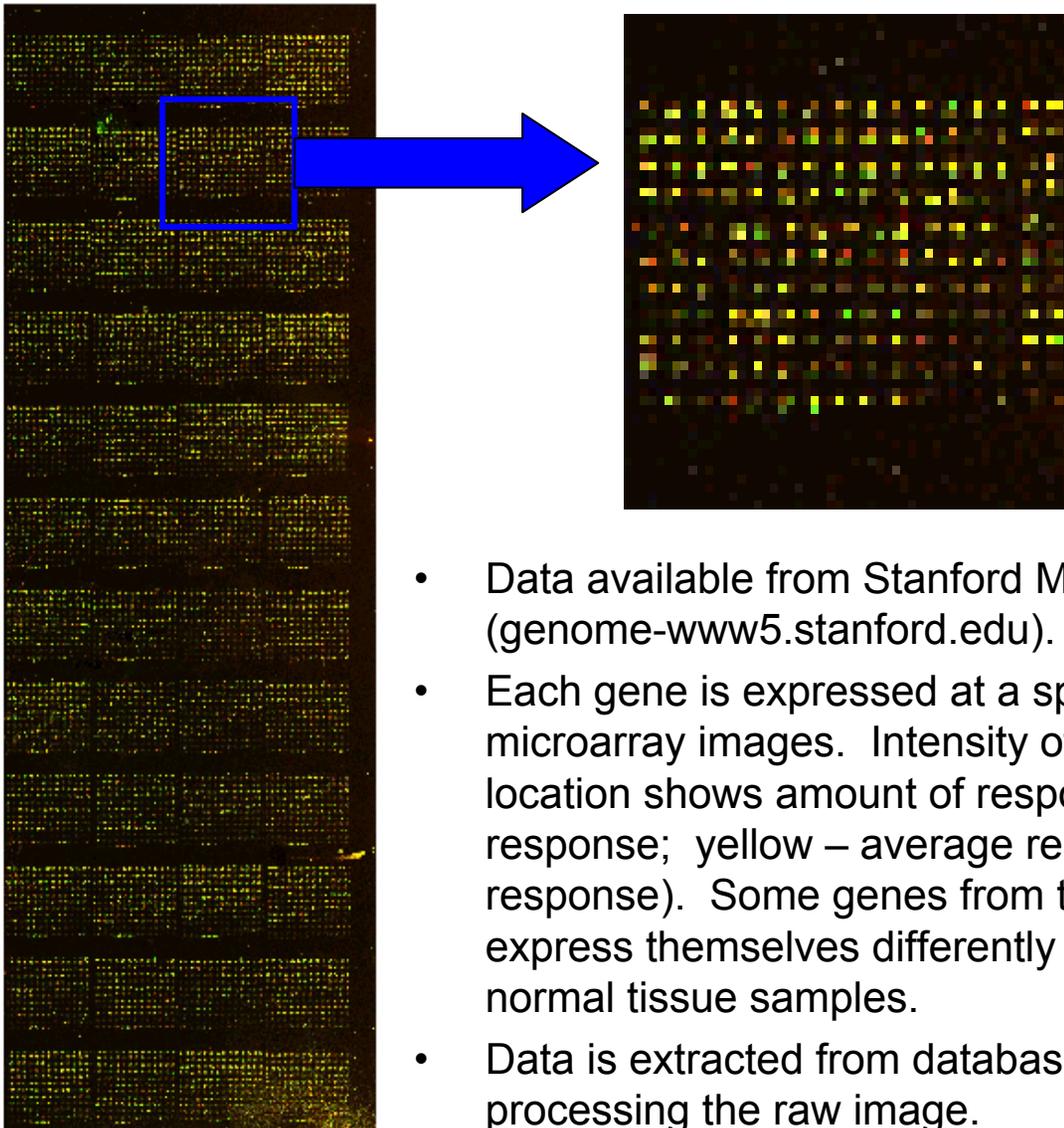
- Assume that the principal component is a linear combination of the snapshots, with weighting factors  $w_i$ .

$$\Phi_I(\vec{x}) = \sum_{i=1}^{n_s} w_i V_i(\vec{x})$$

- The weighting factors can be shown to be the components of the primary eigenvector of the covariance matrix  $\theta$ , where the  $(i,j)$  component of  $\theta$  is defined as:

$$\theta_{i,j} = \frac{1}{n_s} \langle V_i, V_j \rangle, \quad i = 1, \dots, n_s, j = 1, \dots, n_s$$

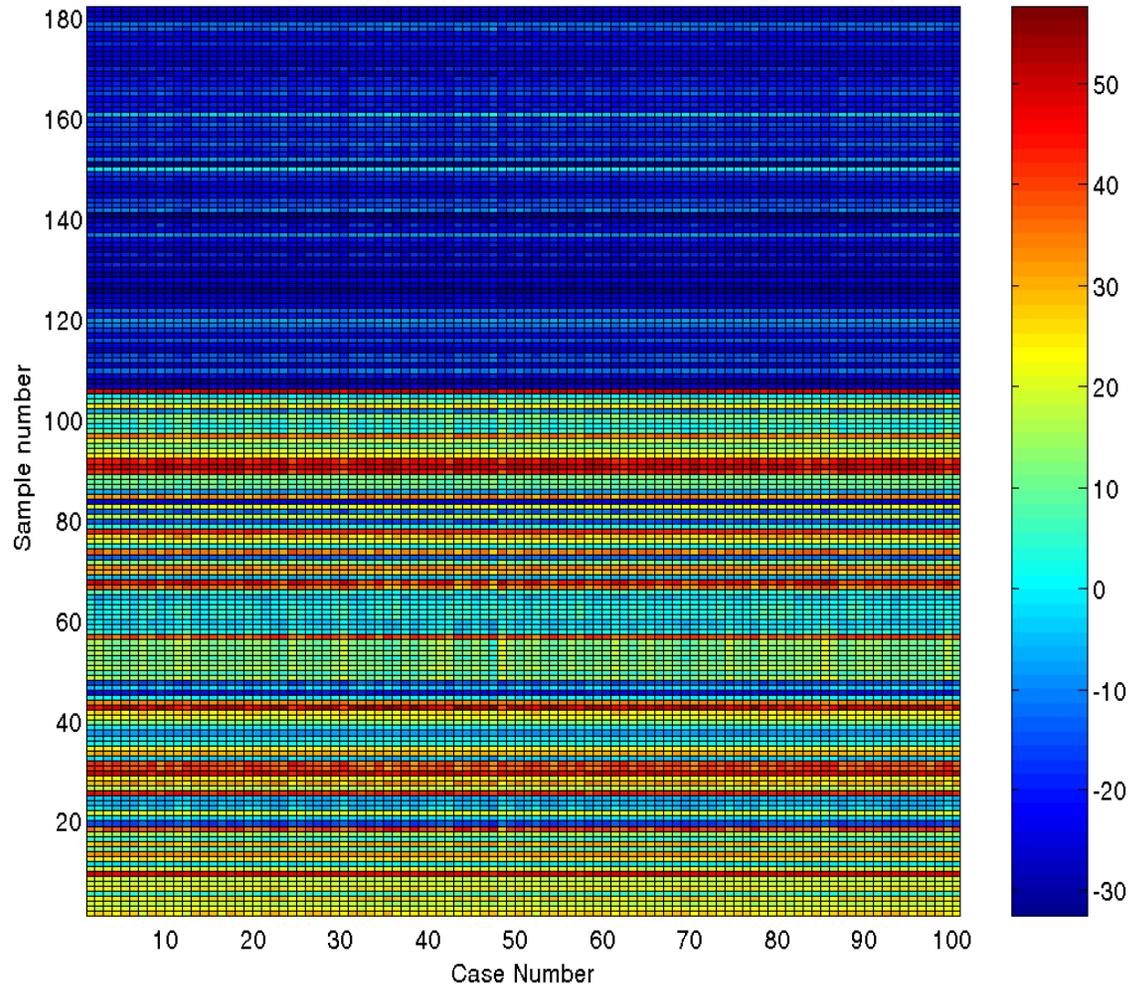




- Data available from Stanford Microarray Database ([genome-www5.stanford.edu](http://genome-www5.stanford.edu)).
- Each gene is expressed at a specific grid location in the microarray images. Intensity of the image at the grid location shows amount of response (green – minimal response; yellow – average response; red – maximal response). Some genes from tumorous samples will express themselves differently than the same genes from normal tissue samples.
- Data is extracted from database in tabular form, rather than processing the raw image.

- Data for analysis was obtained from Chen, Xin, et. al, “Gene Expression Patterns in Human Liver Cancers”, Molecular Biology of the Cell, Vol. 13, 1929-1939, June 2002
- Reference provided DNA data for:
  - **76 normal** tissue samples
  - **105 primary liver tumor** samples.
- Data for **5520 genes** were extracted
  - In order for a gene to be included in this analysis, data for that gene had to be present in at least 80% of the samples
  - If a sample is missing data for a particular gene, the value was imputed by using the mean of the values from the remaining samples.
  - Mean values for each gene were then subtracted off before performing the orthogonal decomposition

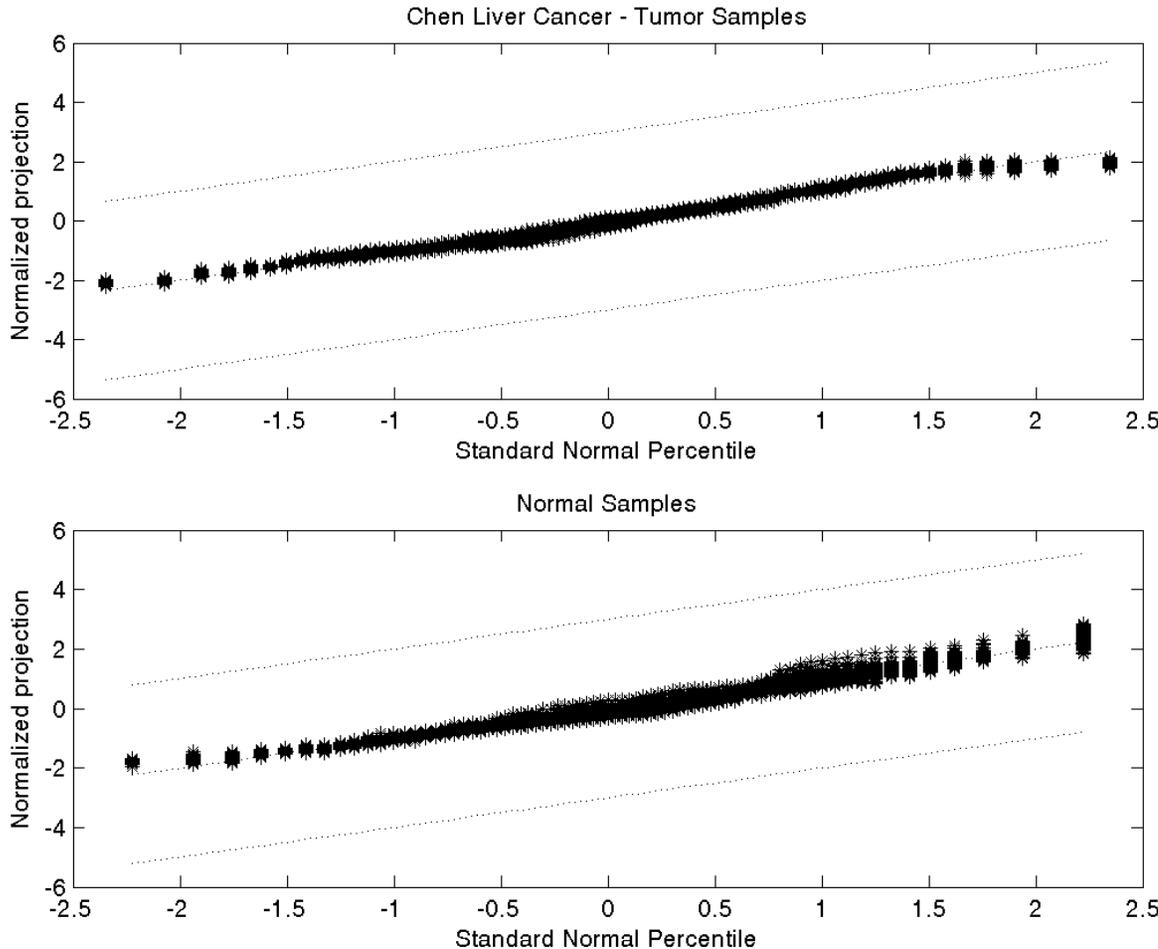
Projections on Principal Component



- **Tumorous tissue samples (1 - 105)**
- **Normal tissue samples (106 - 181)**
- **Principal component analysis performed 100 times**
  - **The principal component was extracted using 85 tumorous tissue samples (selected at random)**
- **Figure shows the projections of the samples onto the principal component**
- **Projections for normal tissue samples are almost always negative.**

# Percentile Limits vs. Standard Normal Distribution

## Chen Liver Cancer Study

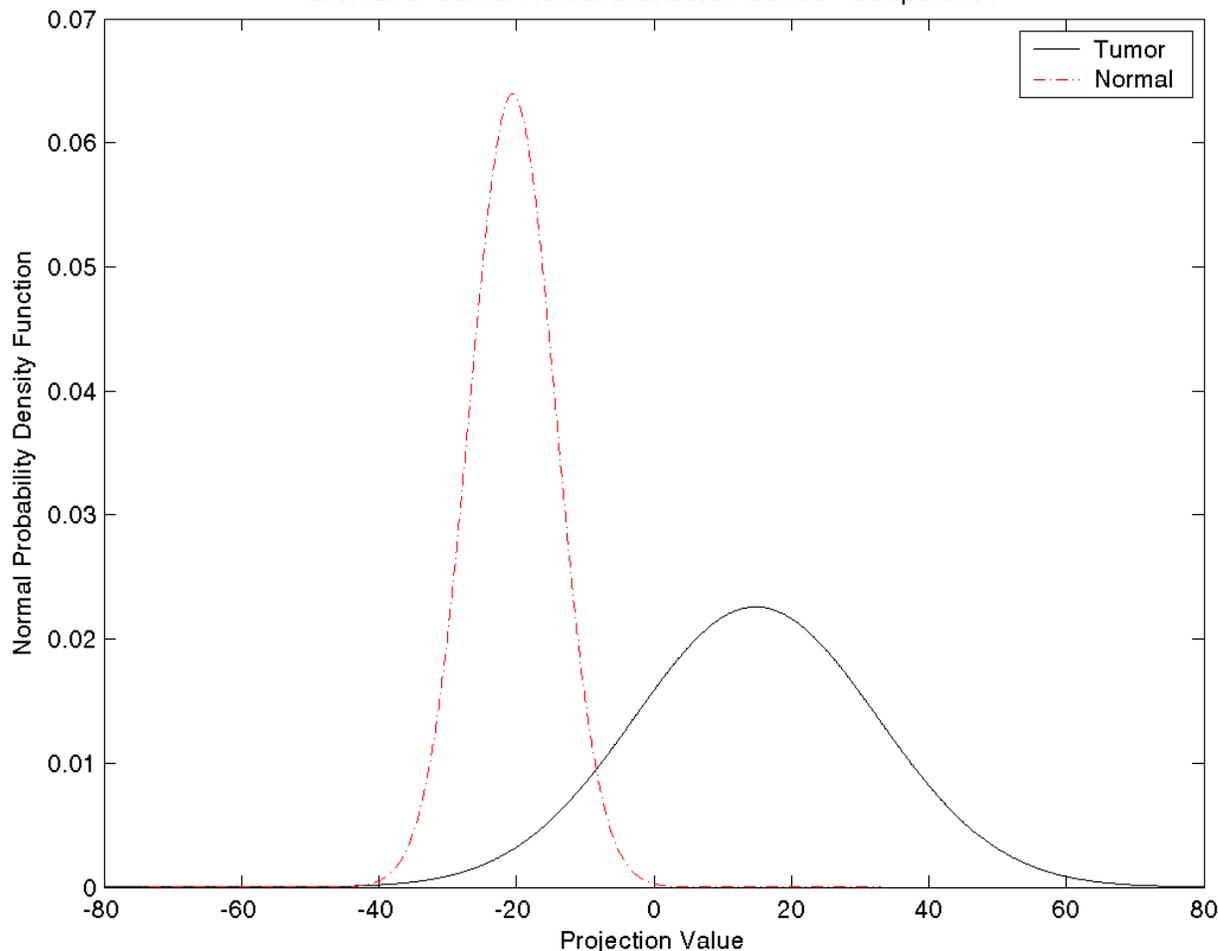


- Projections for a representative case are normalized

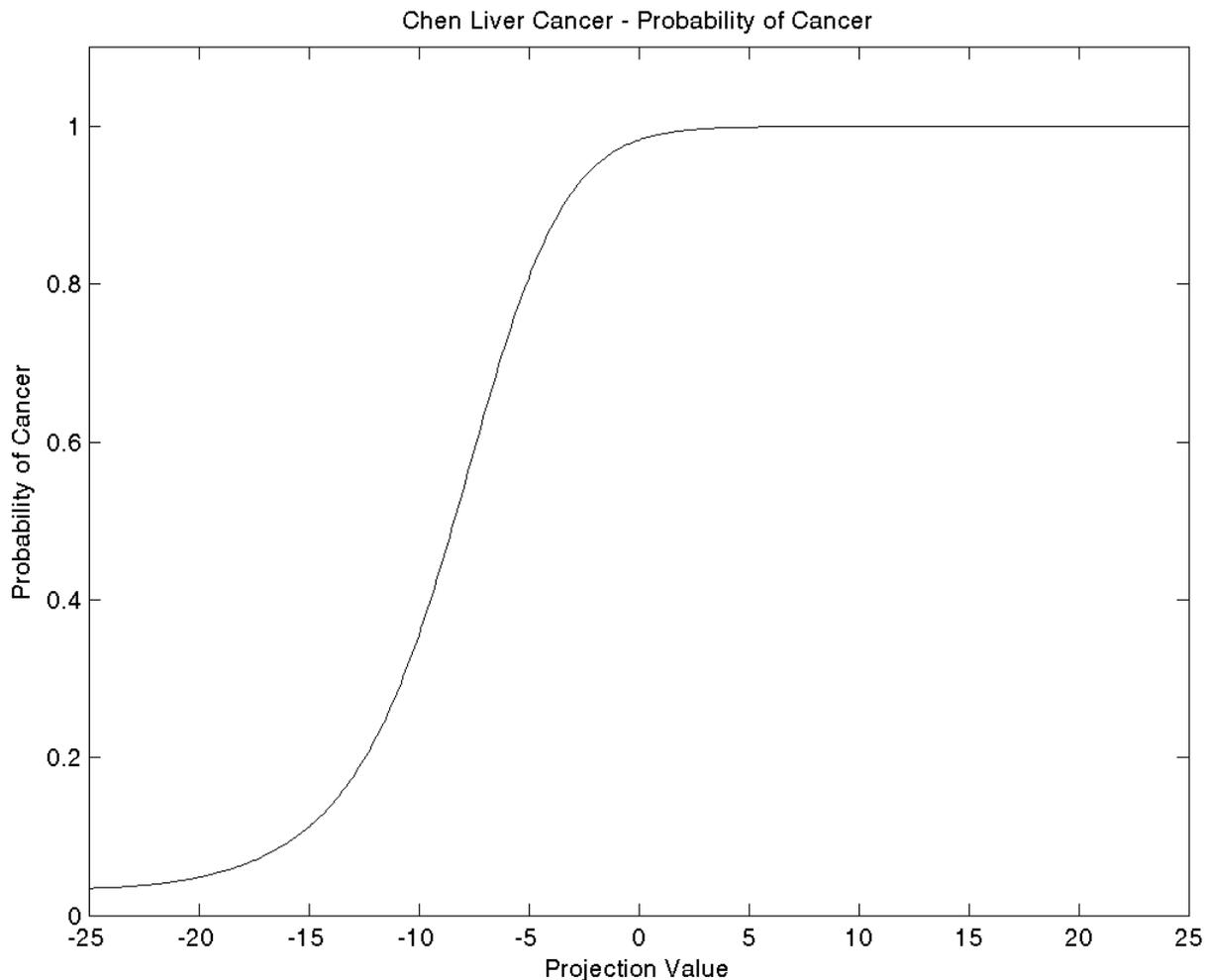
$$\frac{x - \mu}{\sigma}$$

- Percentile values are plotted against percentile values for a standard normal distribution
- If samples are normally distributed, they would tend to align with the line  $y=x$  (center dotted line on plots)

Chen Liver Cancer Normal Distribution Curves - Component 1



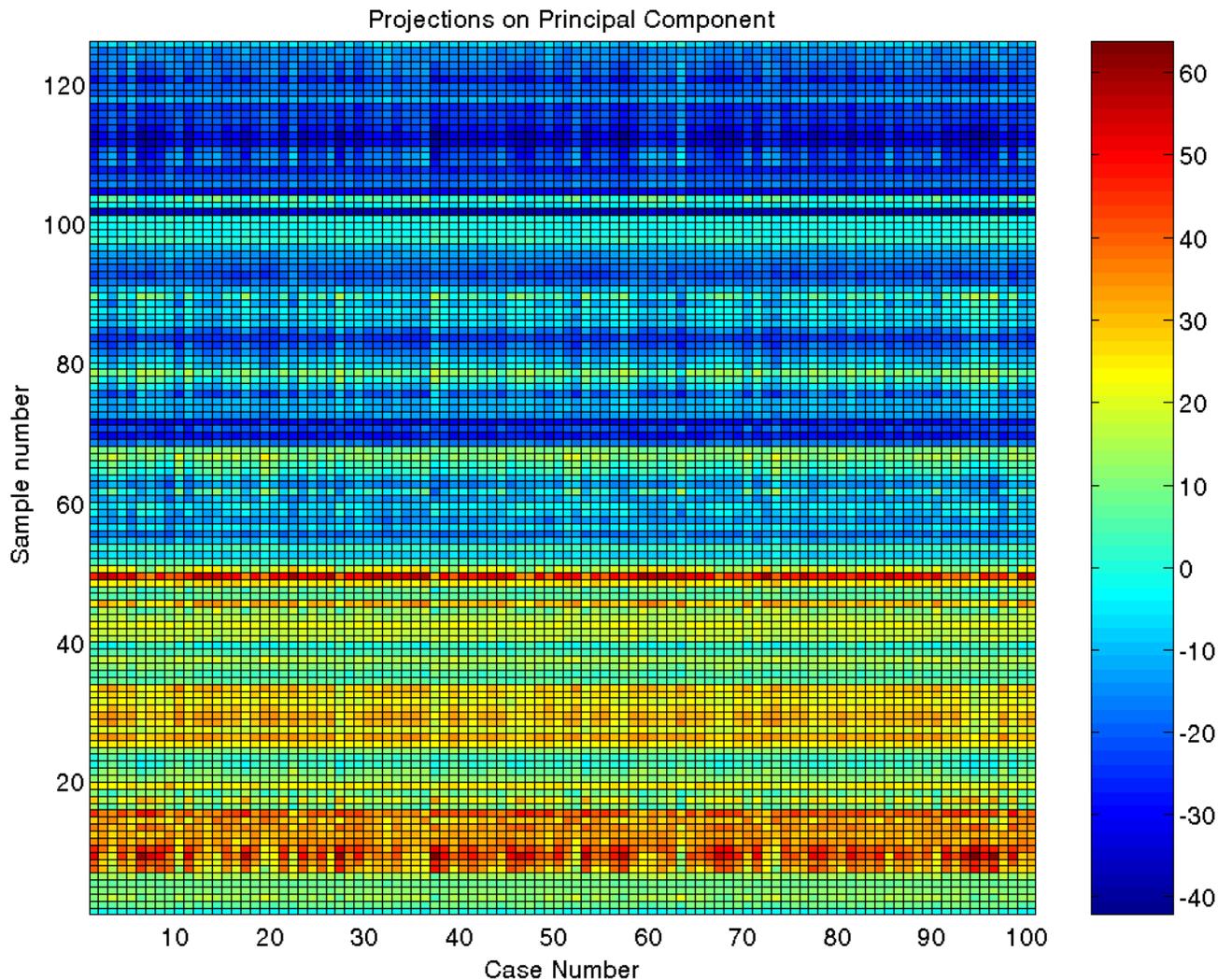
- **Statistics generated for normal and tumorous tissue samples.**
- **Data tended to be normally distributed.**
- **Normal distribution curves are shown here.**
- **If projection is positive, sample is almost certainly tumorous.**
- **If projection is negative, there is approximately a 25% chance that the sample is tumorous.**



- Data for analysis was obtained from Chen, Xin, et. al, “*Variation in Gene Expression Patterns in Human Gastric Cancers*”, Mol Biol Cell. 2003 Aug; 14(8): 3208-15. Epub 2003 Apr 17
- Reference provided DNA data for:
  - **21 normal** tissue samples
  - **103 gastric tumor** samples.
- Data for **6688 genes** were extracted
  - In order for a gene to be included in this analysis, data for that gene had to be present in at least 80% of the samples
  - If a sample is missing data for a particular gene, the value was imputed by using the mean of the values from the remaining samples.
  - Mean values for each gene were then subtracted off before performing the orthogonal decomposition

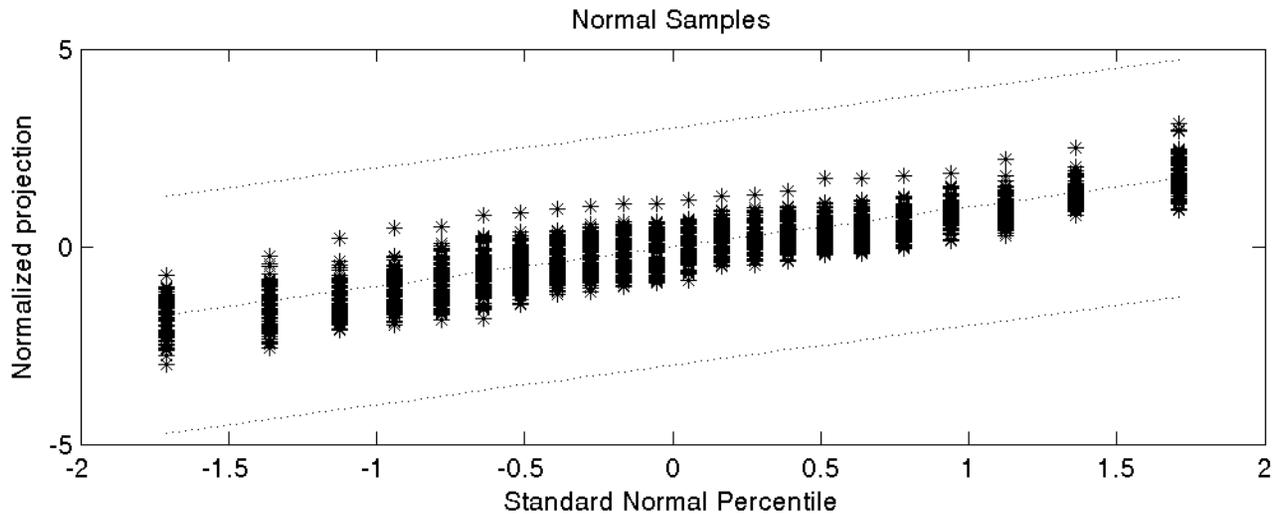
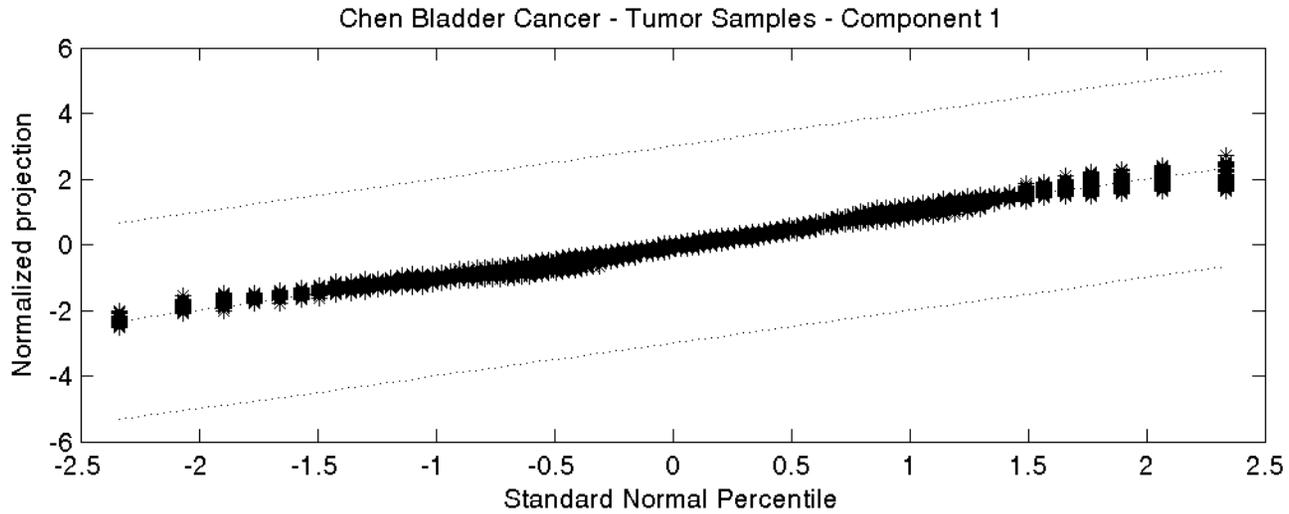
# Projections Onto The Principal Component

Chen Bladder Cancer Study



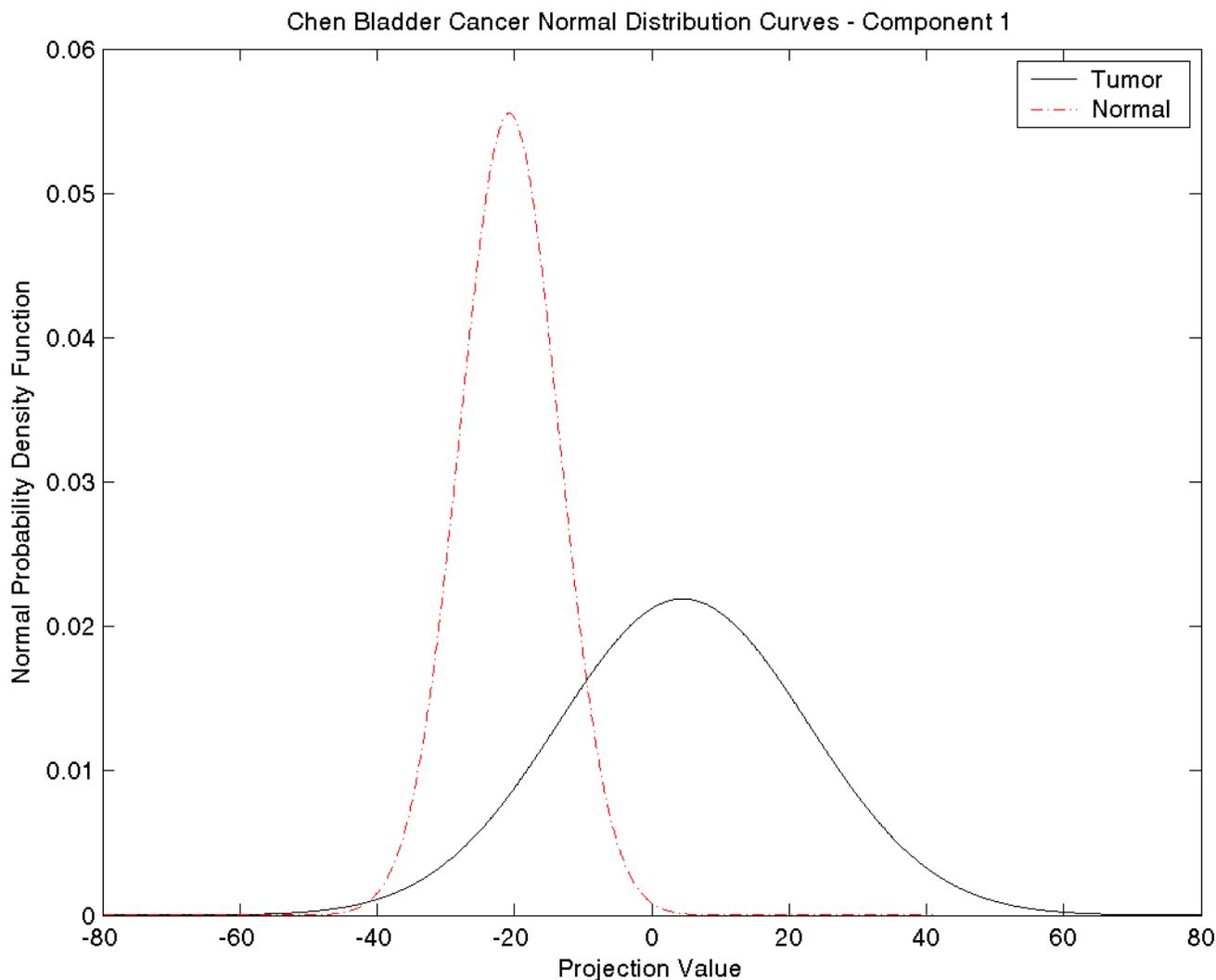
# Percentile Limits vs. Standard Normal Distribution

## Chen Bladder Cancer Study



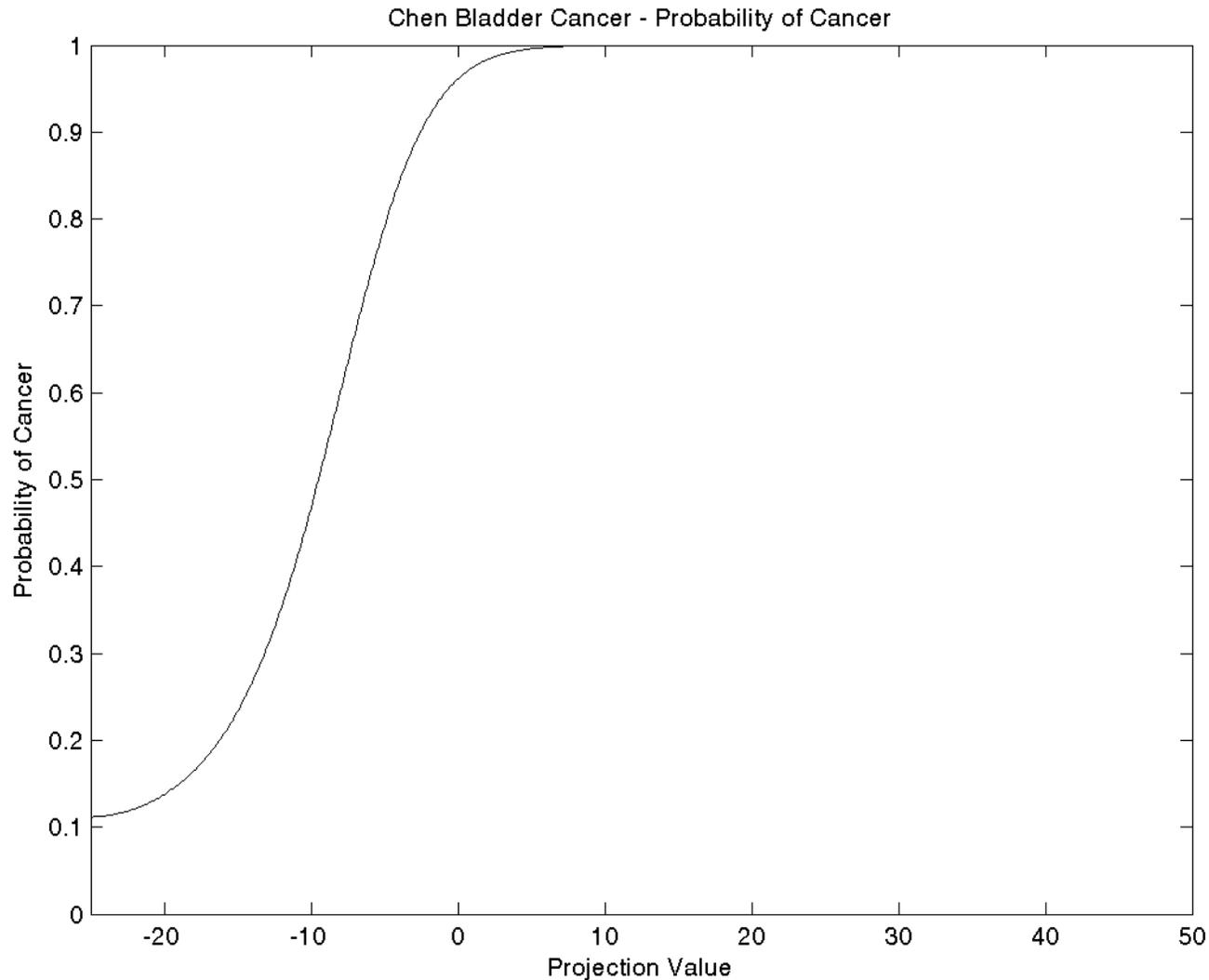
# Normal Distribution Curves

## Chen Bladder Cancer Study



# Probability of Cancer vs. Projection

## Chen Bladder Cancer Study



- Applying Principal Component Analysis techniques to DNA microarray data can be used as a basis for simple disease detection applications.
- The method was demonstrated using data from Chen's liver and gastric cancer studies, although the method is general and could be applied to any type of disease.
- The case study presented in this analysis showed that the method could be prone to false negatives.
- Increased reliability of the method might be achieved by including more components, other than just the principal component, in the analysis
- Future work could also involve more efficient numerical (matrix free) methods to allow processing of more samples/more genes.

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