Peak Modeling for Ion Mobility Spectrometry Measurements

Dominik Kopczynski

Collaborative Research Center SFB 876,
Computer Science XI, TU Dortmund, Germany

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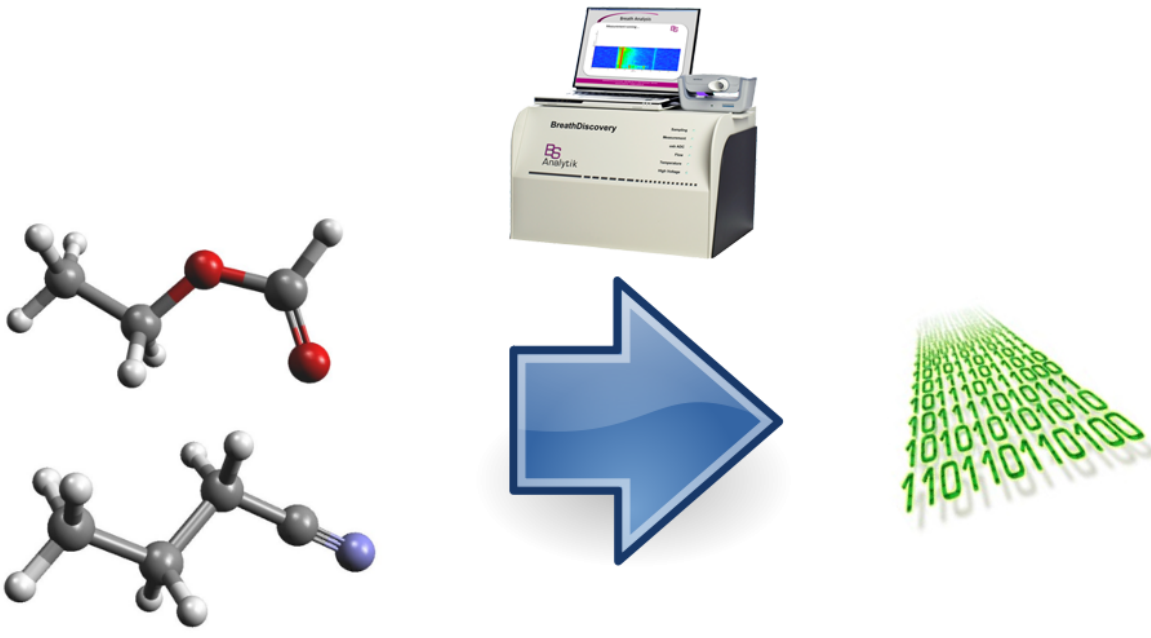
Ion mobility spectrometry (IMS)



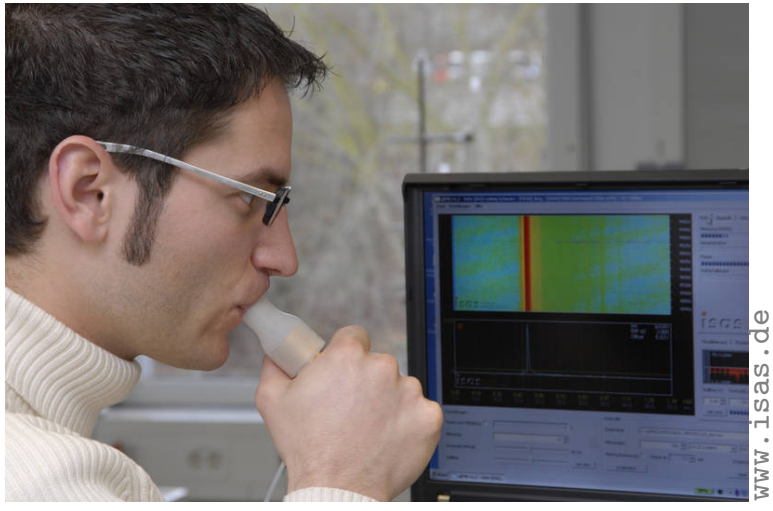
IMS measurement

IMS functionality

- Analyzes concentration of compounds in air
- Works with ambient pressure in contrast to mass spectrometry
- Measurement takes $\approx 25\,\text{ms}$

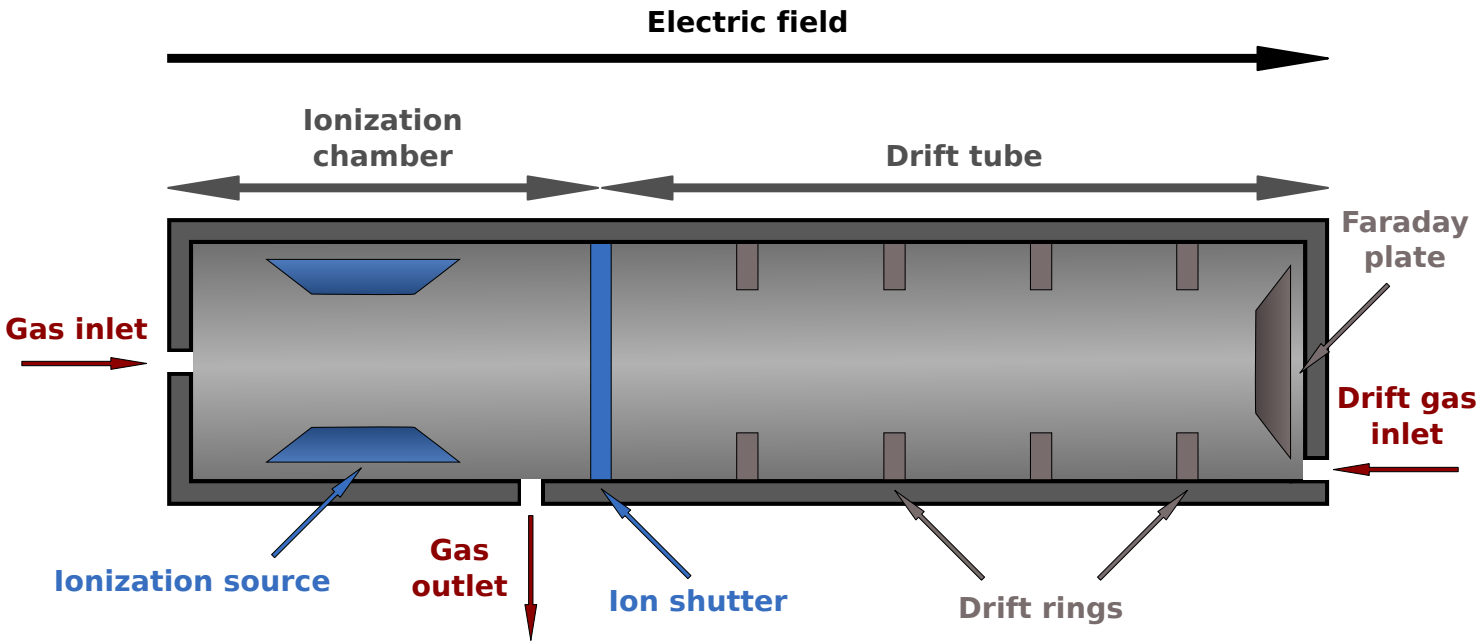
Application areas

Detecting drugs and explosives in airports



Breath gas analysis in medicine *(main reasearch)*

Cross section of IMS device



Multi-capillary column

MCC functionality

- About 1 200 columns
- Gel-coated on inside
- Mobile phase: molecules pushed by carrier gas
- Stationary phase: molecules stick to gel
- Time to cross: retention time (in s)

Coupling MCC with IMS device

After 0 sec:

- MCC: dimension in retention time (in s)
- IMS: dimension in drift time (in ms)

Coupling MCC with IMS device

After 2 sec:

- MCC: dimension in retention time (in s)
- IMS: dimension in drift time (in ms)

Coupling MCC with IMS device

After 5 sec:

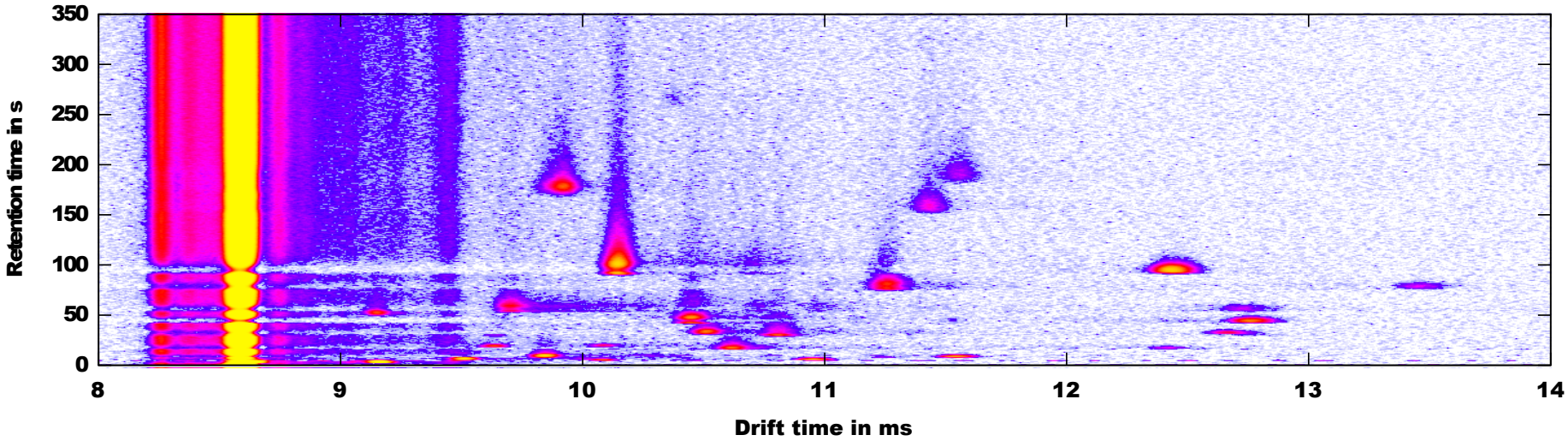
- MCC: dimension in retention time (in s)
- IMS: dimension in drift time (in ms)

Coupling MCC with IMS device

After 10 sec:

- MCC: dimension in retention time (in s)
- IMS: dimension in drift time (in ms)

Heatmap of MCC/IMS measurement



- About 3 000 000 data points
- Peak location: compound type
- Peak intensity: compound concentration
- Peaks are potential biomarkers

Clustering and estimating parameters

Approch

- First approach: cluster data points *(k-means)*

Approch

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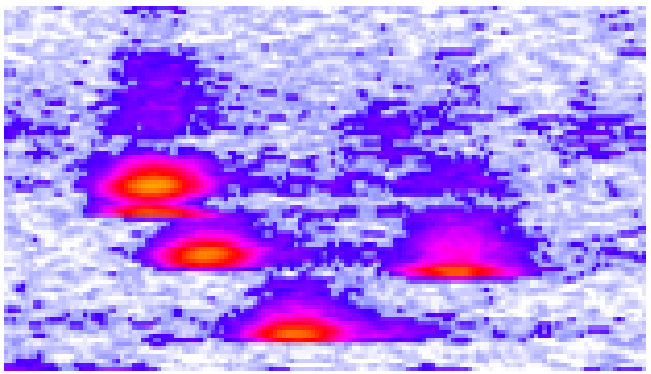
- Problem: peaks can overlap, hard-clustering impossible



Approch

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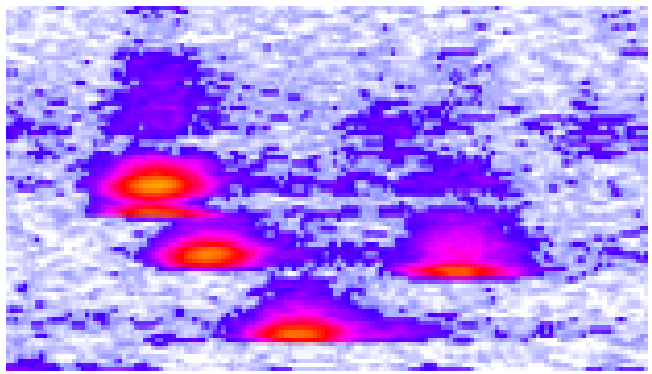

- Solution: soft-clustering with statistical models

Analysis method

Approach

- Set up likelihood function
- Use **Expectation Maximization (EM) algorithm** to maximize likelihood

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EM algorithm

- Method to estimate parameters for statistical models
- Soft clustering $\Rightarrow$ peak decomposition
- Always finds local optimum

EM algorithm

Expectation step

- Given: $|R| \times |T|$ data points and $1 \leq j \leq c$ models
- Estimate hidden values $W_{(r,t),j}$ describing membership of every datapoint to every model

EM algorithm

Expectation step

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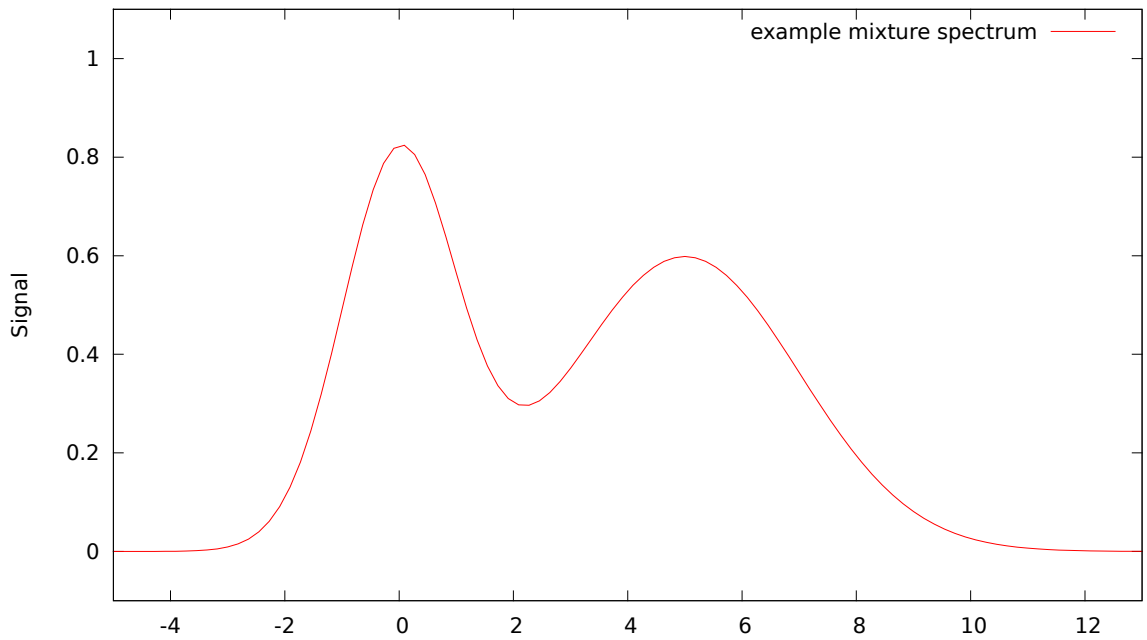
- Estimate hidden values $W_{(r,t),j}$ describing membership of every datapoint to every model

Maximization step

- Estimate weight of model in relation to whole measurement
- Use maximum likelihood estimators (MLE) to estimate parameters for every model

EM example



- Given:
  - n datapoints i.e. mixture model
  - supposed statistical distribution
- Find: estimated parameters for models

Setting up ...

Notation

- s_i = signal at coordinate $x_{1 \leq i \leq n}$
- $1 \leq j \leq c$ models
- $W_{i,j}$ = membership for x_i to model j
- ω = normalized weight for model j in measurement
- Θ = parameter vector for distribution
- $P_{\Theta_j}(x_i)$ = p.d.f. of distribution

Likelihood

$$L_{x,W}(\Theta, \omega) = \prod_i^n \prod_j^c \left[\omega_j \cdot P_{\Theta_j}(x_i)\right]^{s_i \cdot W_{i,j}}$$

Setting up ... (cont'd)

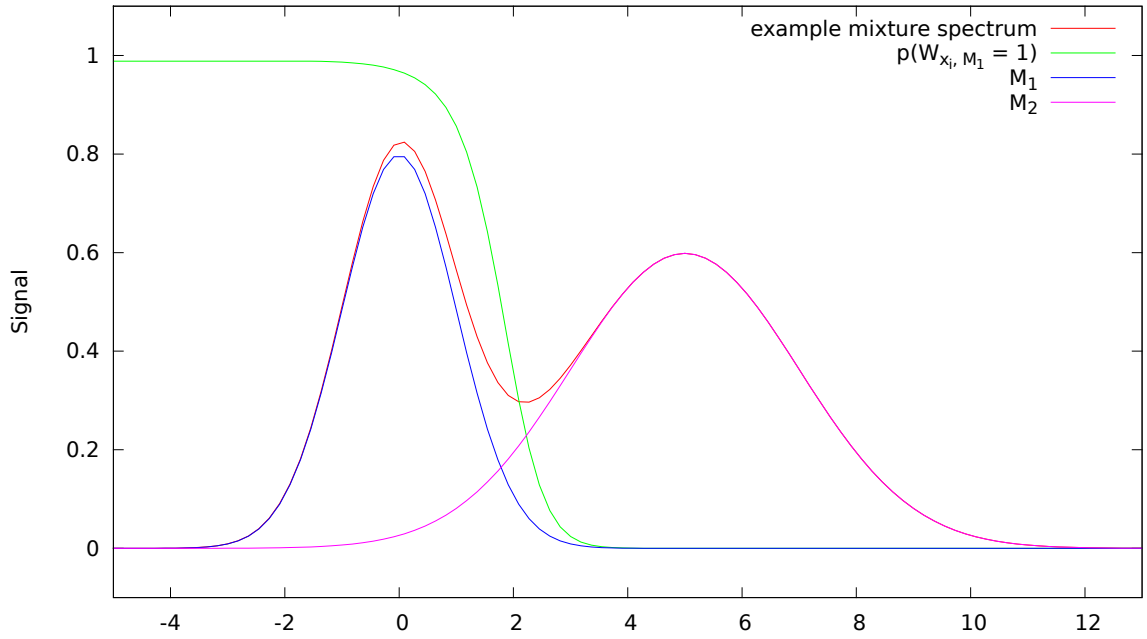
log likelihood

$$\mathcal{L}_{x,W}(\Theta,\omega) = \sum_{i}^{n} s_i \sum_{j}^{c} W_{i,j} \cdot \log\left(\omega_j \cdot P_{\Theta_j}(x_i)\right)$$

Maximum likelihood estimators

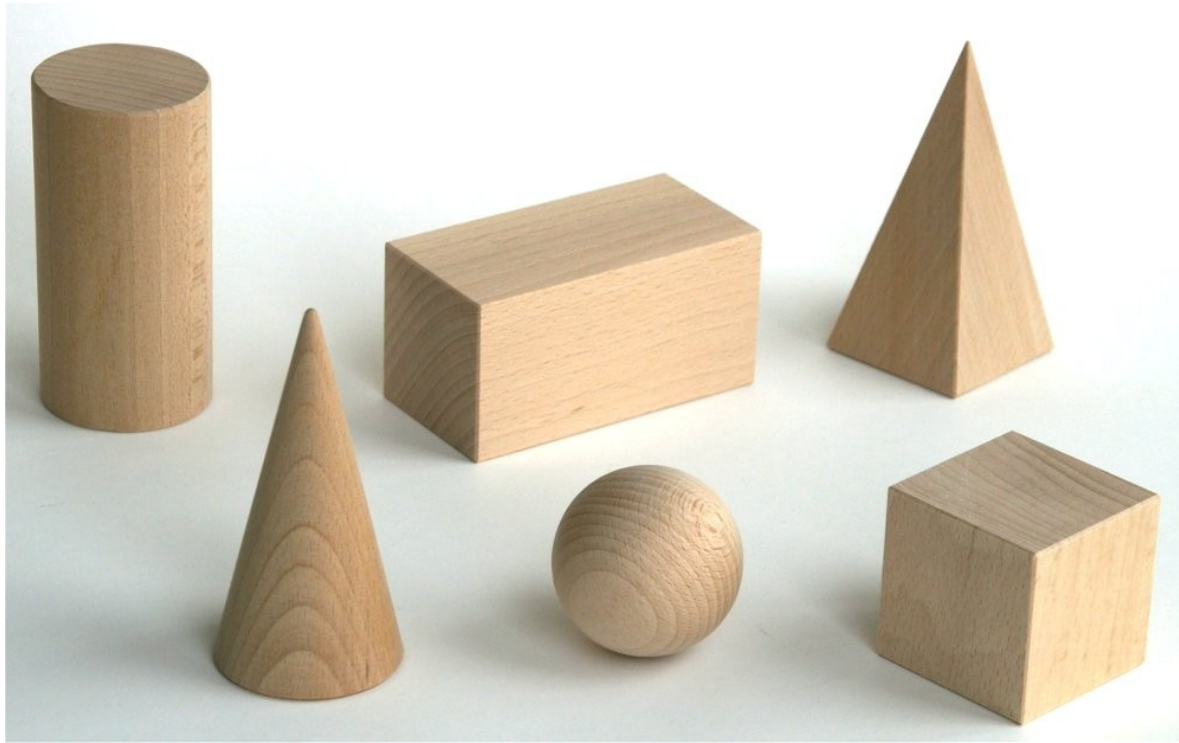
- $W^0_{i,j} = \frac{\omega_j \cdot P_{\Theta_j}(x_i)}{\sum_{k}^{c} \omega_k \cdot P_{\Theta_k}(x_i)}$
- $\omega^*_j = \frac{1}{n} \sum_{i}^{n} W^0_{i,j}$
- MLE for model parameters depend on model

EM example (cont'd)

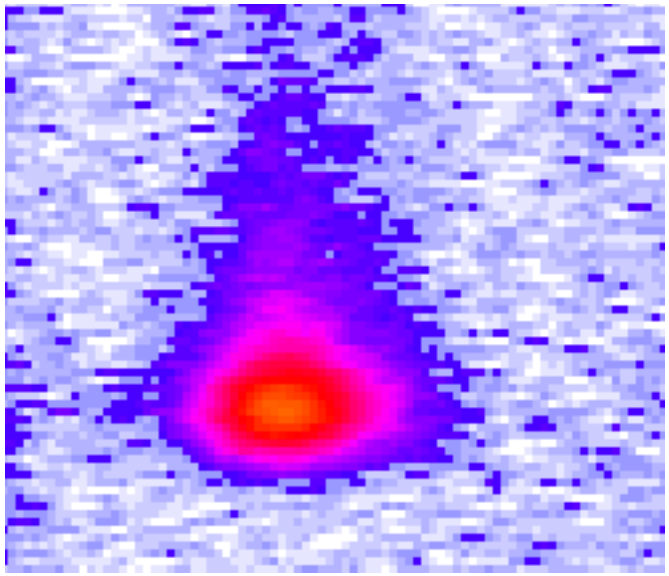


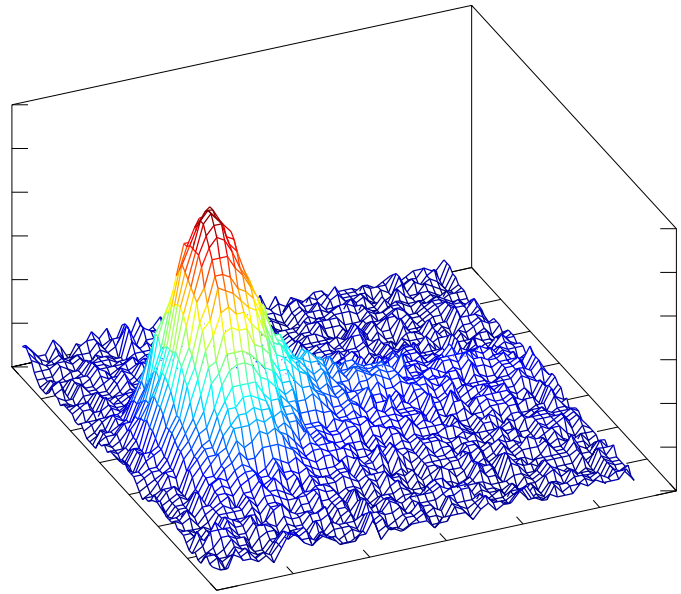
- $M_1 : \mu_1 = 0, \sigma_1 = 1, \omega_1 = 0.4$
- $M_2 : \mu_2 = 5, \sigma_2 = 2, \omega_2 = 0.6$

Describing peaks



Peaks

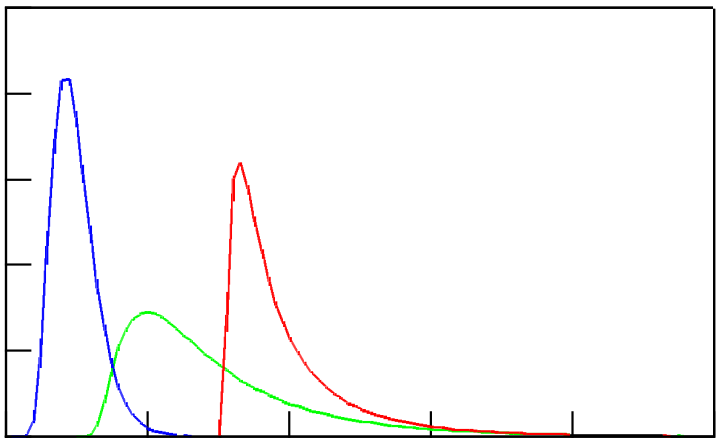




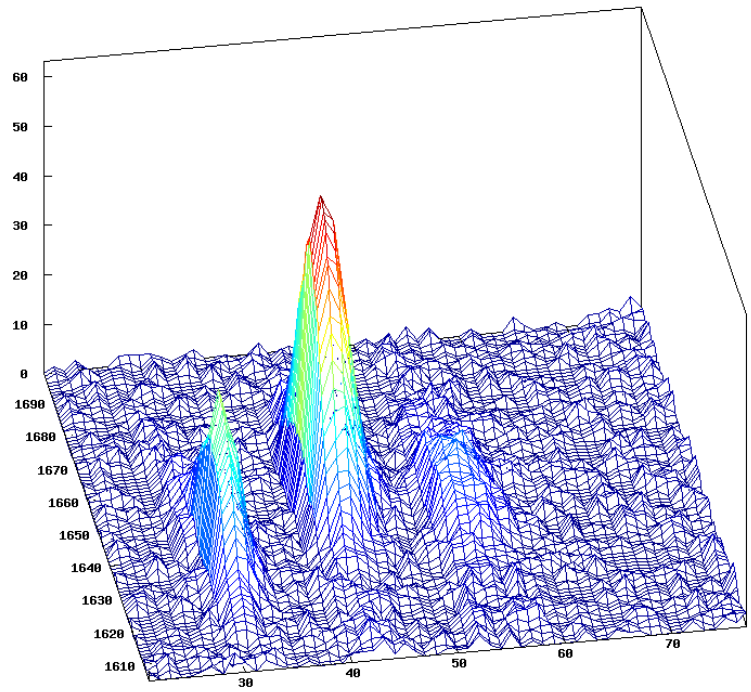
- Peaks can consist of thousands of datapoints
- Skewed in retention and drift time

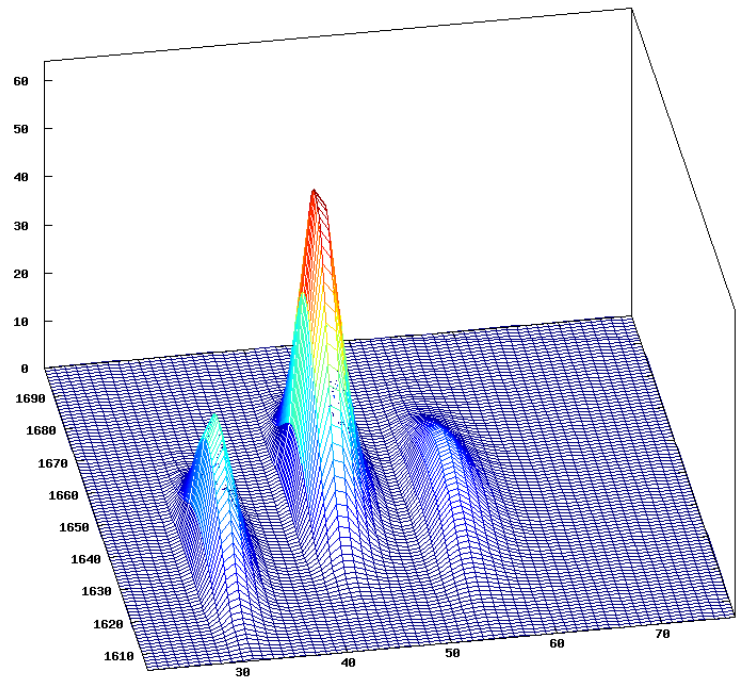
Statistical model to describe peaks

- Two-dimensional distribution model
- Inverse Gaussian distribution in retention and drift time
- $IG(x|\mu,\lambda,o) = \sqrt{\frac{\lambda}{2\pi(x-o)^3}} \exp\left(-\frac{\lambda(x-o-\mu)^2}{2\mu^2(x-o)}\right)$
- Model $M = \omega \cdot IG(\mu_r,\lambda_r,o_r) \cdot IG(\mu_t,\lambda_t,o_t)$
- Seven parameters per model
- No physical explanation, phenomenologically fits well



Example Result



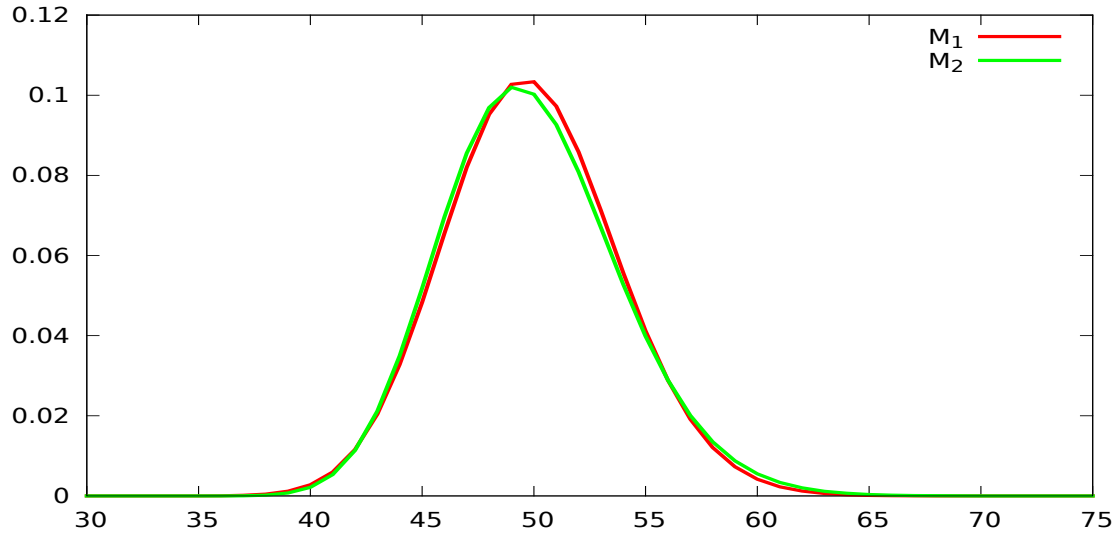


- Input: 600 datapoints
- Output: 21 parameters
- For whole measurement: data reduction factor $\approx 10\,000$

Parameter comparability

http://www.teaching-learning.eu

Model parameters not comparable



Model	μ	λ	o
M_1	71.2	24344.3	-21.3
M_2	35.2	2779.8	14.7

- Large differences caused by offset parameter o
- Search for descriptors with similar values on similar models

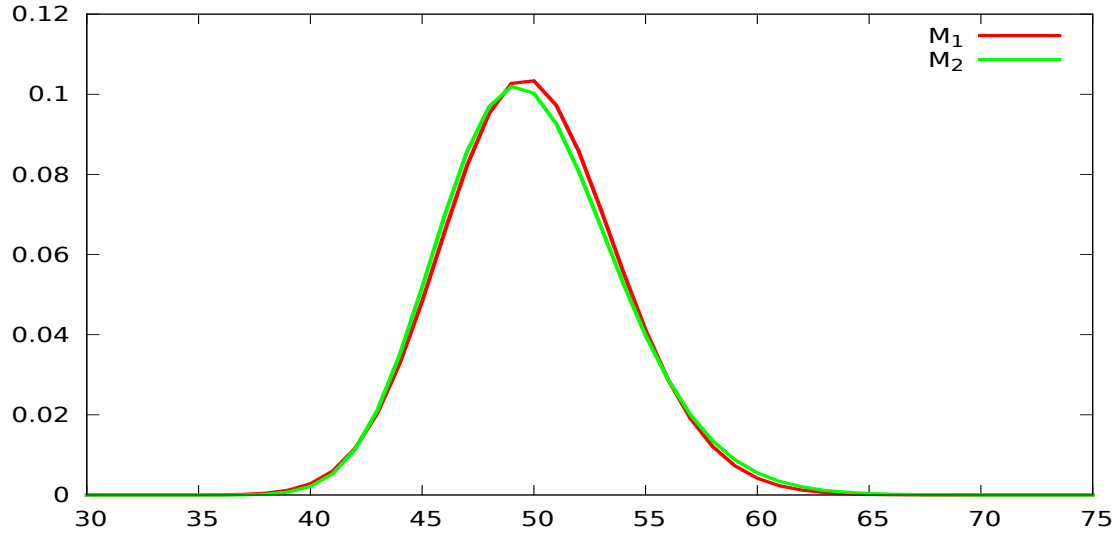
Find appropriate descriptors

Use similar descriptors instead of model parameters:

- Uncorrected mean $\mu' = \mu + o$
- Standard deviation $\sigma = \sqrt{\frac{\mu^3}{\lambda}}$
- Mode $m = \mu \left(\sqrt{1 + \frac{9\mu^2}{4\lambda^2}} - \frac{3\mu}{2\lambda} \right) + o$

Model parameters simply recomputable from descriptors

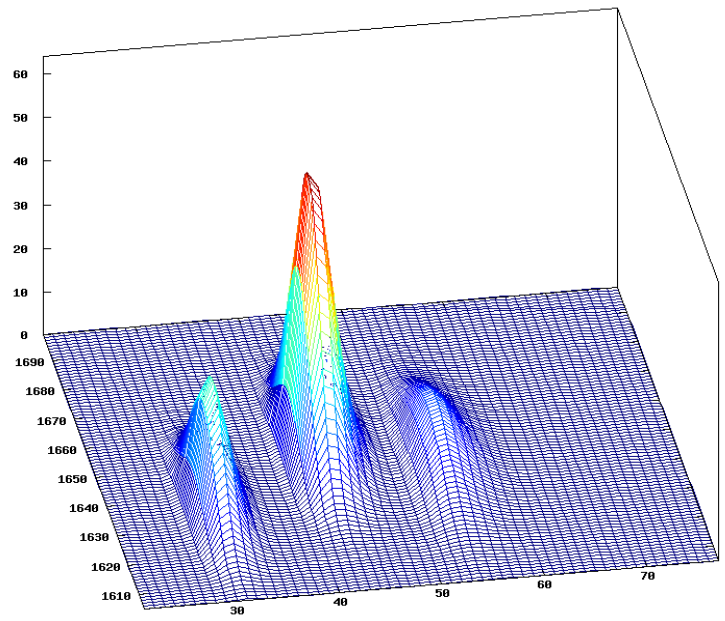
Descriptors

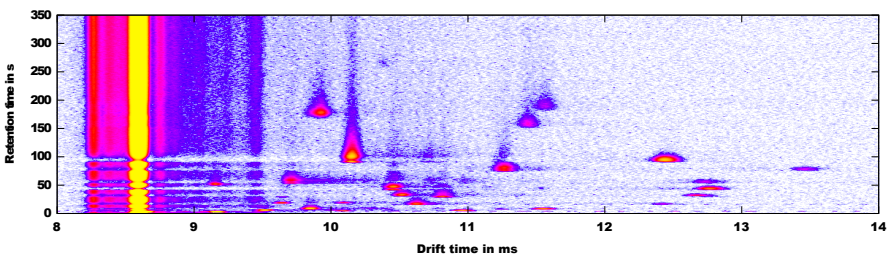


Model	μ	λ	o	μ'	σ	m
M_1	71.2	24344.3	-21.3	49.90	3.85	49.58
M_2	35.2	2779.8	14.7	49.90	3.96	49.23

Summary

- Describe peaks with statistical models
- EM algorithm for parameter estimation
- Reduction factor: $\approx 10\,000$





- Descriptors:
  - More intuitive
  - Make peaks comparable

Thanks to SFB 876 - TB1 project members

- Project leaders:
  - Sven Rahmann (Uniklinikum Essen / TU Dortmund)
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