Towards automation of chromatographic data treatment: a Bayesian approach

Gabriel Vivó Truyols, Michael Woldegebriel
Van ‘t Hoff institute for molecular sciences
University of Amsterdam

Automation is our challenge now...

Why Bayesian?

Evolution of the instrumentation

1 bit

GC: 1 KB

HPLC: 1KB

GC-MS; ~100 KB

HPLC-DAD; ~100 KB

HPLC-MS;
1 MB

GCxGC: ~100 KB

GCxGC-MS;
LCxLC-MS;
1 GB/hour

GCxGC-HRMS;
LCxLC-HRMS;
15 GB/hour

Automation using a frequentist approach

Why Bayesian?

Data + *Algorithm* = *Information*

$$\sum \theta \sin \epsilon$$

There is a chromatographic peak at t_R=12 min.

These 10 peaks in these 10 chromatograms belong to the same compound.

… etc.

In a sense, the machines are "taking responsibility" on the decision…

… and only the final result is shown.

Automation using a frequentist approach

Why Bayesian?

Final result

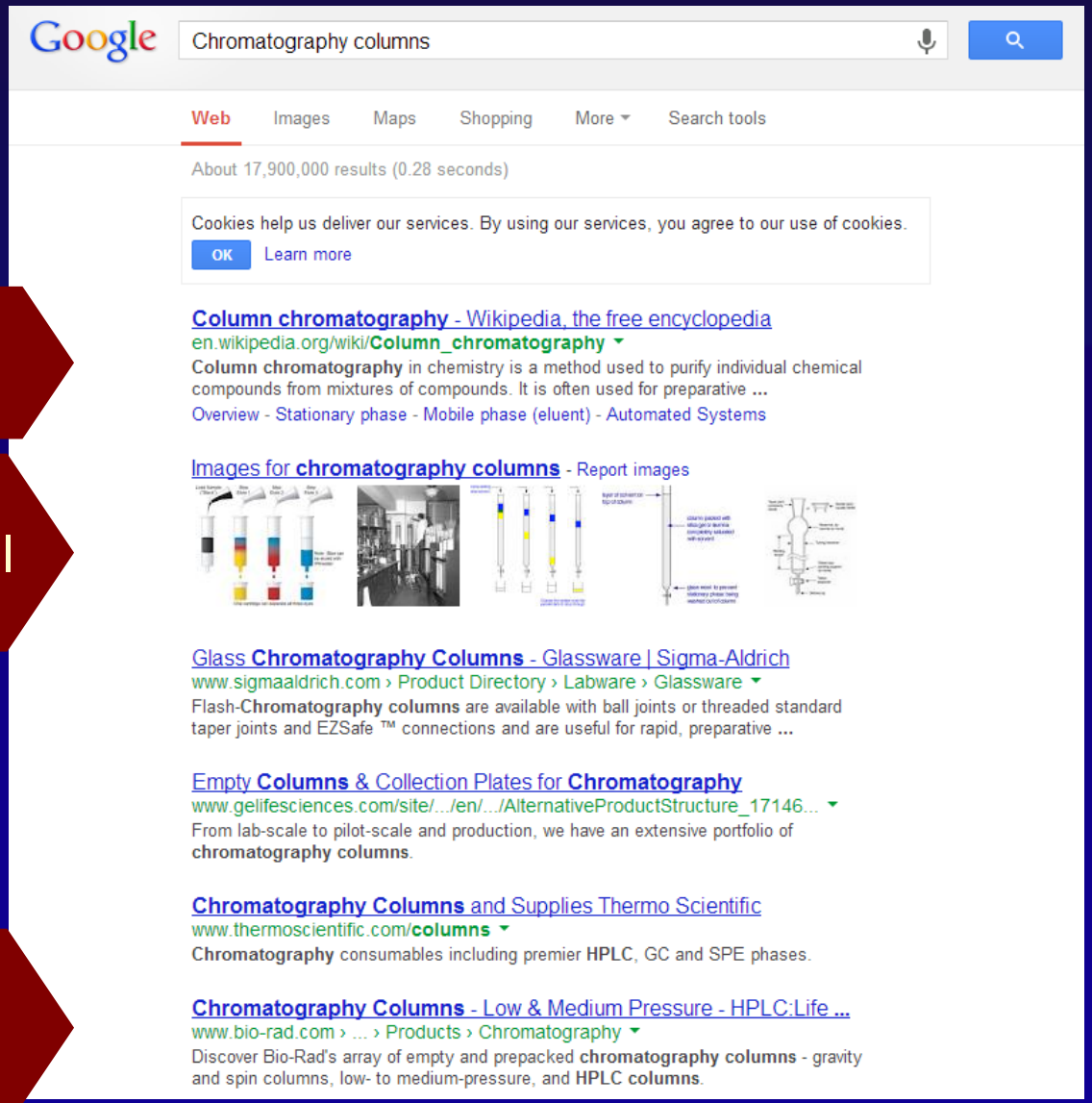
Automation using a "Bayesian" approach

Why Bayesian?

Most likely result

Less likely result (but still possible)

…



Automation using a Bayesian approach

Why Bayesian?

Data

87% chance: There is a peak centred at t_R=12 min.

13% chance: There is no peak centred at t_R=12 min.

20% chance: Peaks 1-9 belong to the same compound. Peak 10 is different.

15% chance: Peaks 1-5,7-9 belong to the same compound. Peaks 6 and 10 are different.

… etc.

Information

There is a chromatographic peak at t_R=12 min.

These 10 peaks in these 10 chromatograms belong to the same compound.

a collection of all possibilities (ranked by their probability)

In a sense, the machines are ~~"taking~~ not responsibility" on the decision…

… and only the final result is shown.

It is up to the chromatographer to take the final decision

Bayesian statistics in court

Why Bayesian?

Posterior odds = Likelihood ratio x Prior odds

$$\frac{p(H_0|\mathrm{D})}{p(H_1|\mathrm{D})} = \frac{p(\mathrm{D}|H_0)}{p(\mathrm{D}|H_1)} \times \frac{p(H_0)}{p(H_1)}$$

The suspect is innocent

The suspect is guilty

The scientist does not decide upon the validity of H_0 or H_1, only calculates the likelihood ratio (the value of the evidence)

Bayesian statistics in data automation

Why Bayesian?

Posterior odds = Likelihood ratio x Prior odds

$$\frac{p(H_0|\mathrm{D})}{p(H_1|\mathrm{D})} = \frac{p(\mathrm{D}|H_0)}{p(\mathrm{D}|H_1)} \times \frac{p(H_0)}{p(H_1)}$$

I take the decision!!

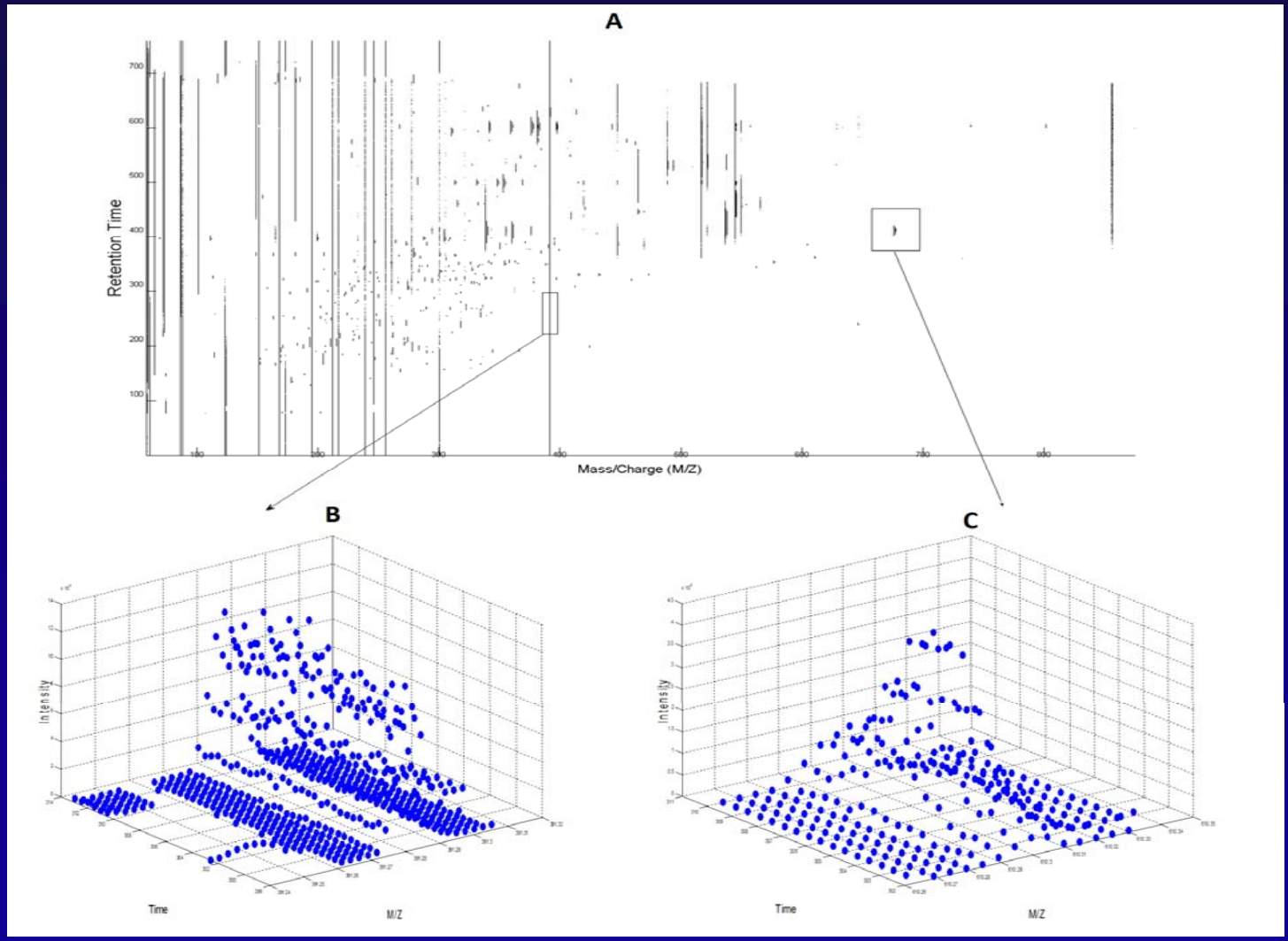
The data is only used to "update" our prior probability on a situation (**but the decision is not "taken" by the algorithm**)

Prior experiments
Bibliographic information

Some practical applications in chromatography

Example I: peak detection in LC-MS

Example I



M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS

Example I

What is the probability
that a certain point is affected
by a chromatographic peak?

The point IS affected by a chromatographic peak → H_1

The point IS NOT affected by a chromatographic peak → H_2

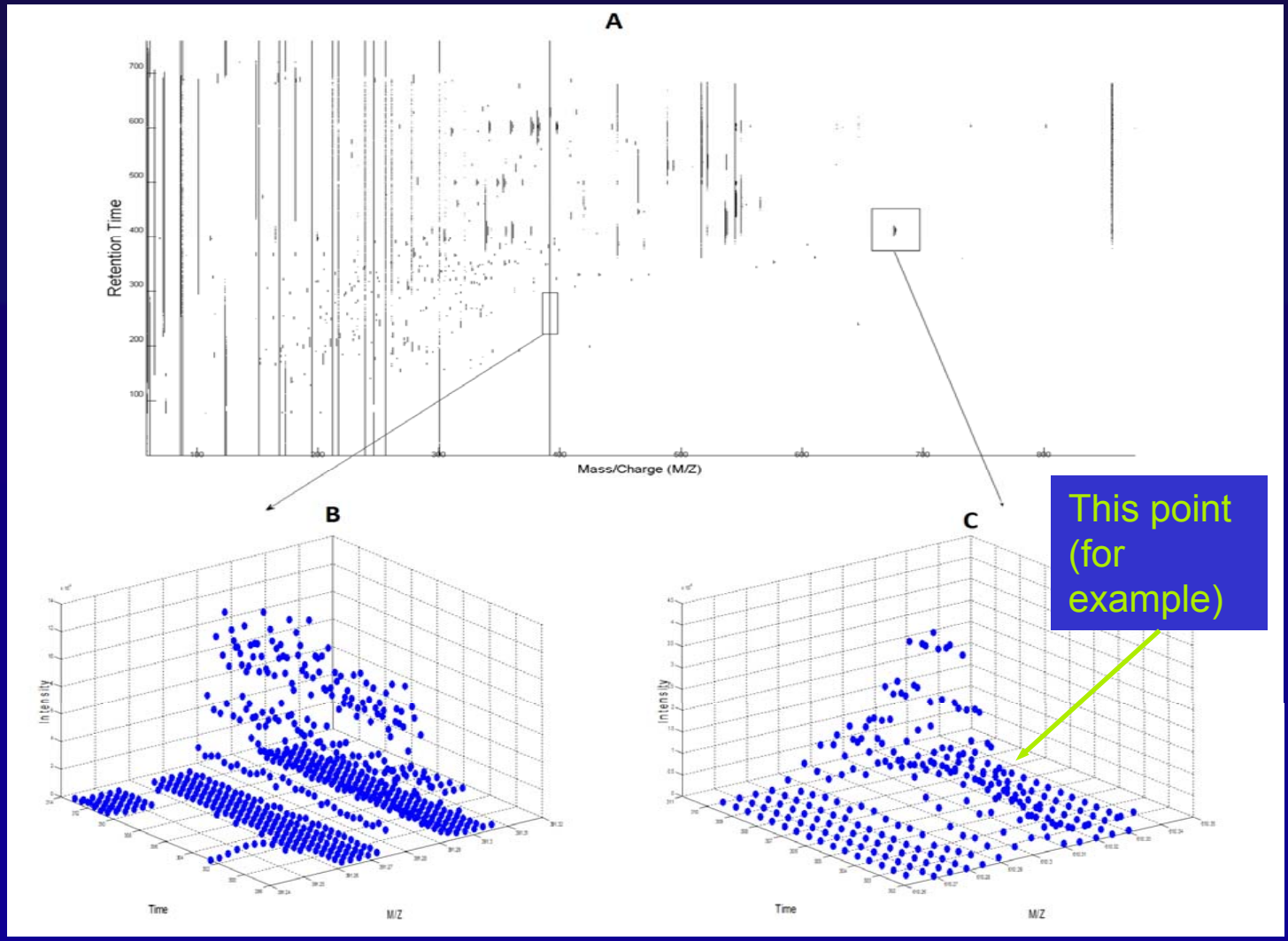
Posterior odds = Likelihood ratio x Prior odds

$$\frac{p(H_1|\mathrm{D})}{p(H_2|\mathrm{D})} = \frac{p(\mathrm{D}|H_1)}{p(\mathrm{D}|H_2)} \times \frac{p(H_1)}{p(H_2)}$$

M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS

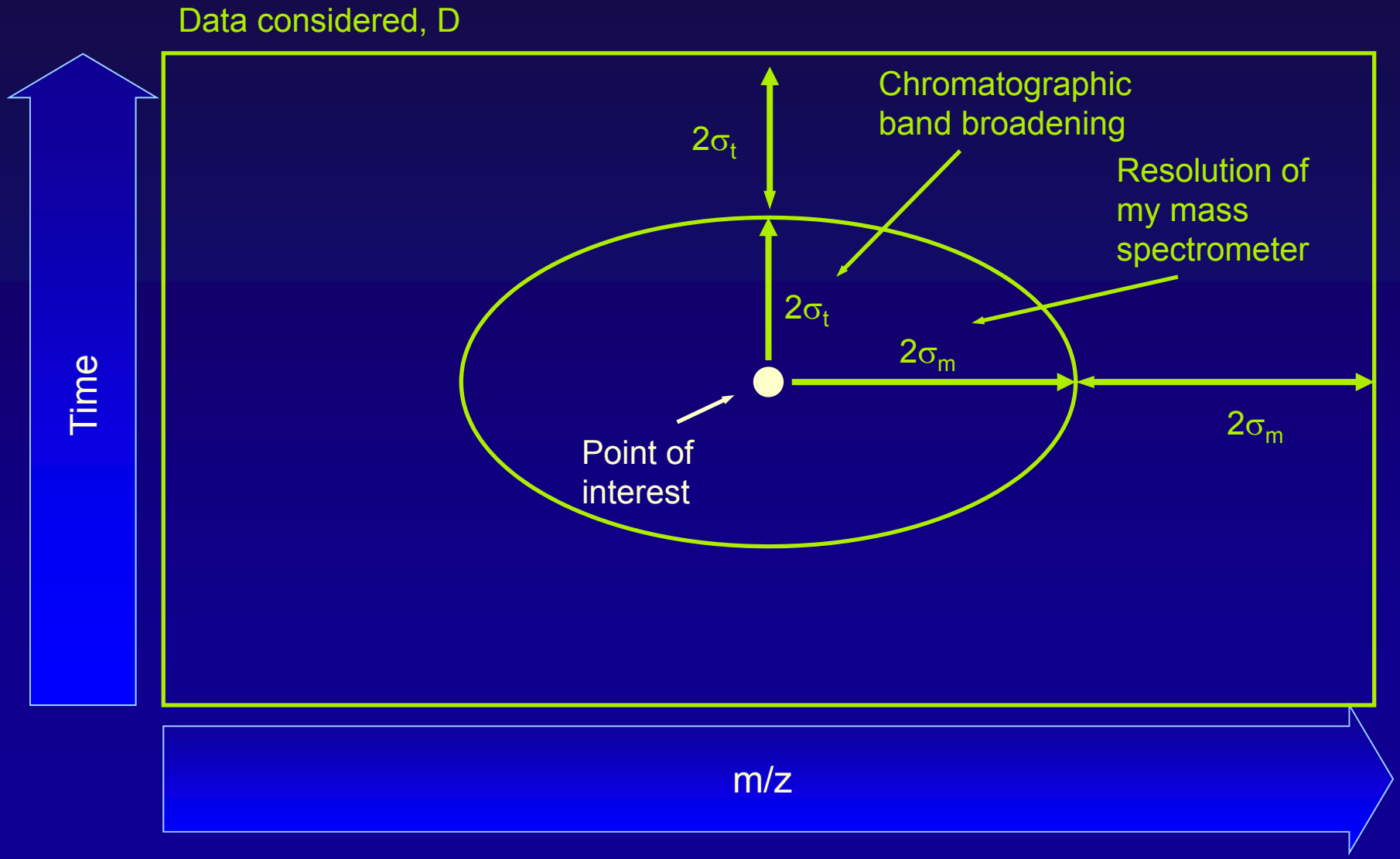
Example I



M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS

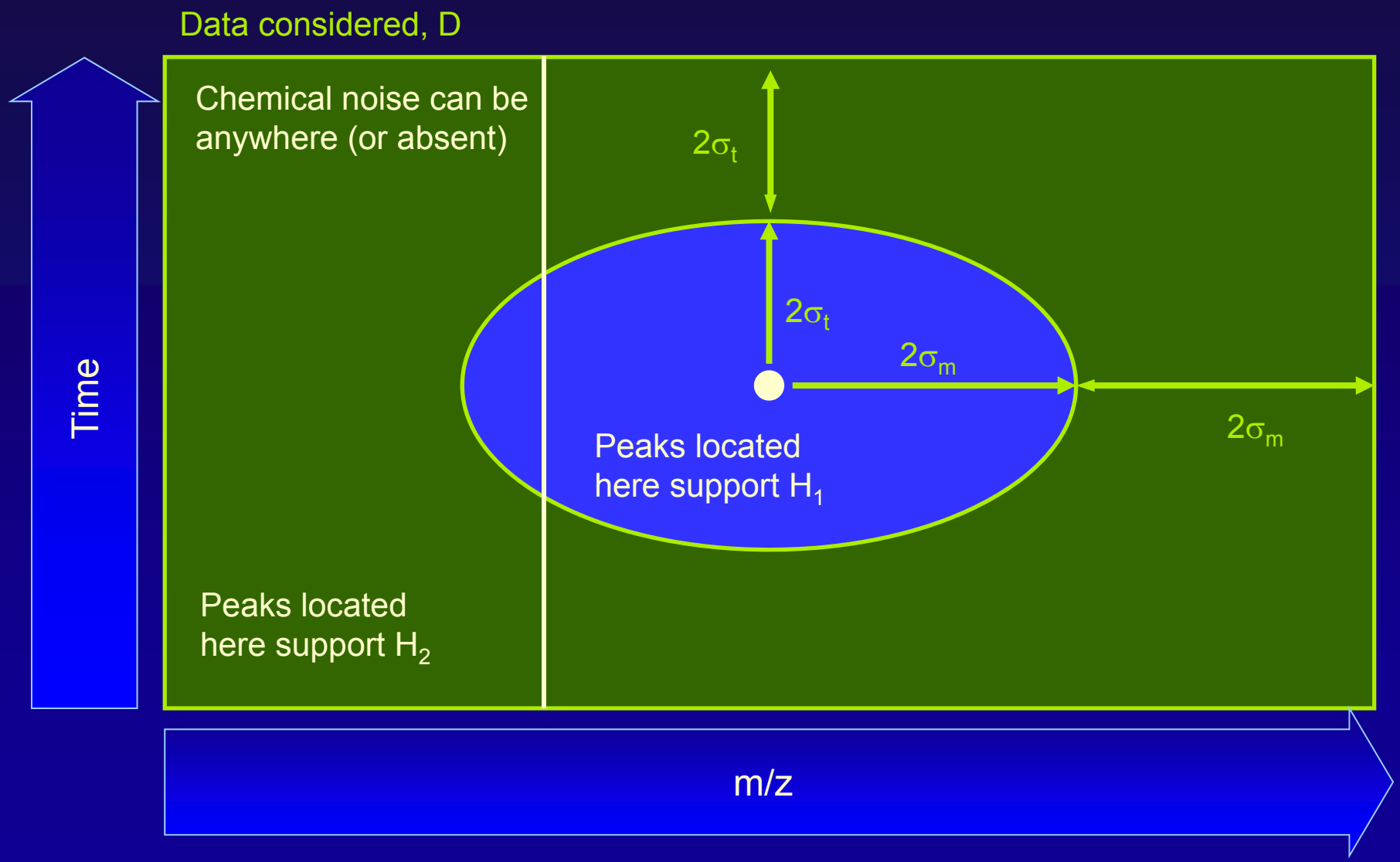
Example I



M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS

Example I



M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I

Example I: peak detection in LC-MS

Likelihood ratio

$$\frac{p(\mathrm{D}|H_1)}{p(\mathrm{D}|H_2)}$$

The point is affected by a peak

The point is not affected

Number of models that support H_1

???

$$p(\mathrm{D}|H_1) = \sum_{\mathrm{w}\in \mathrm{H}_1}^{\mathrm{n1}} \mathrm{P}(\mathrm{D},\mathrm{w}|\mathrm{H}_1) = \sum_{\mathrm{w}\in \mathrm{H}_1}^{\mathrm{n1}} \mathrm{P}\left(D\middle|\mathrm{w},\mathrm{H}_1\right)\mathrm{P}(\mathrm{w}|\mathrm{H}_1)$$

Model case

Number of models that support H_2

$$p(\mathrm{D}|H_2) = \sum_{\mathrm{w}\in \mathrm{H}_2}^{\mathrm{n2}} \mathrm{P}(\mathrm{D},\mathrm{w}|\mathrm{H}_2) = \sum_{\mathrm{w}\in \mathrm{H}_2}^{\mathrm{n2}} \mathrm{P}\left(D\middle|\mathrm{w},\mathrm{H}_2\right)\mathrm{P}(\mathrm{w}|\mathrm{H}_2)$$

M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS

Example I

$$P(w|H_1) = \frac{\lambda^{n_w} e^{-\lambda}}{n_w!} K$$

Normalization factor

Average number of peaks in D

Maximum number of peaks for model case w

How "crowded" is my chromatogram?

J.M. Davis and J.C. Giddings, Statistical overlap theory, Anal. Chem., 55 (1983).

Total number of peaks / peak capacity

$$P(H_2) = e^{(-M/n_c)} K'$$

Normalization factor

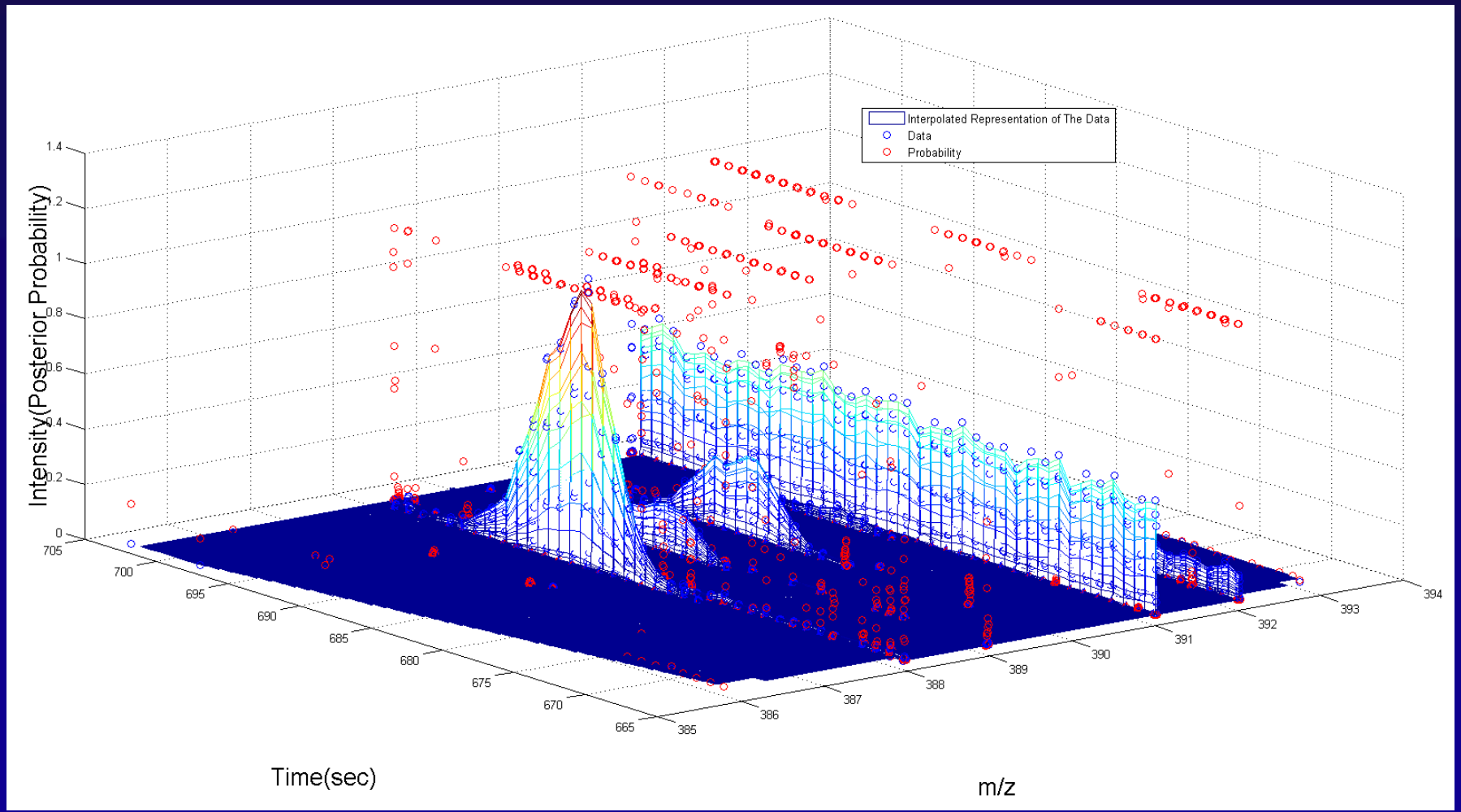
Priors

$$P(H_1) = 1 - P(H_2)$$

M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS. Results

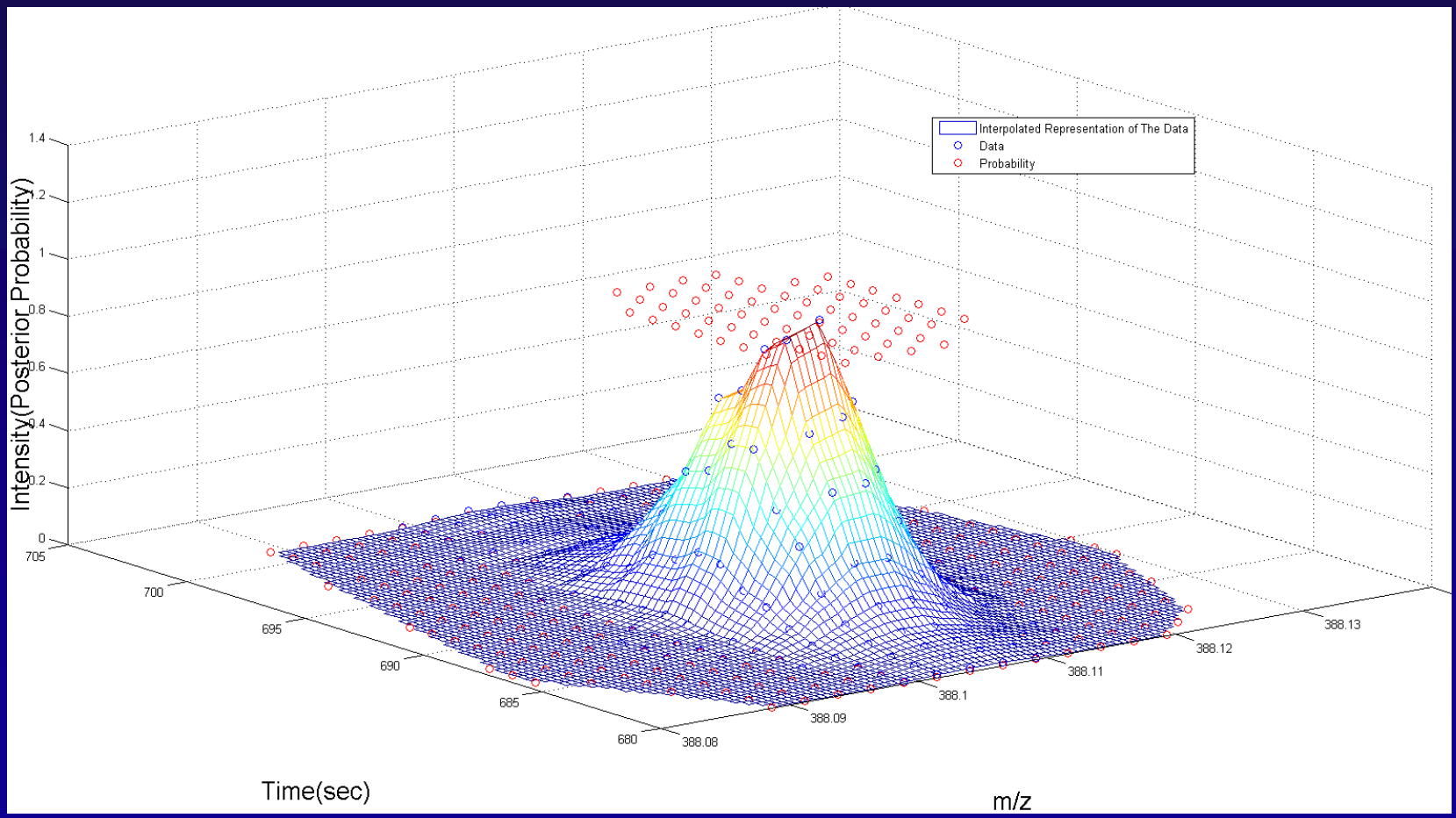
Example I



M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS. Results

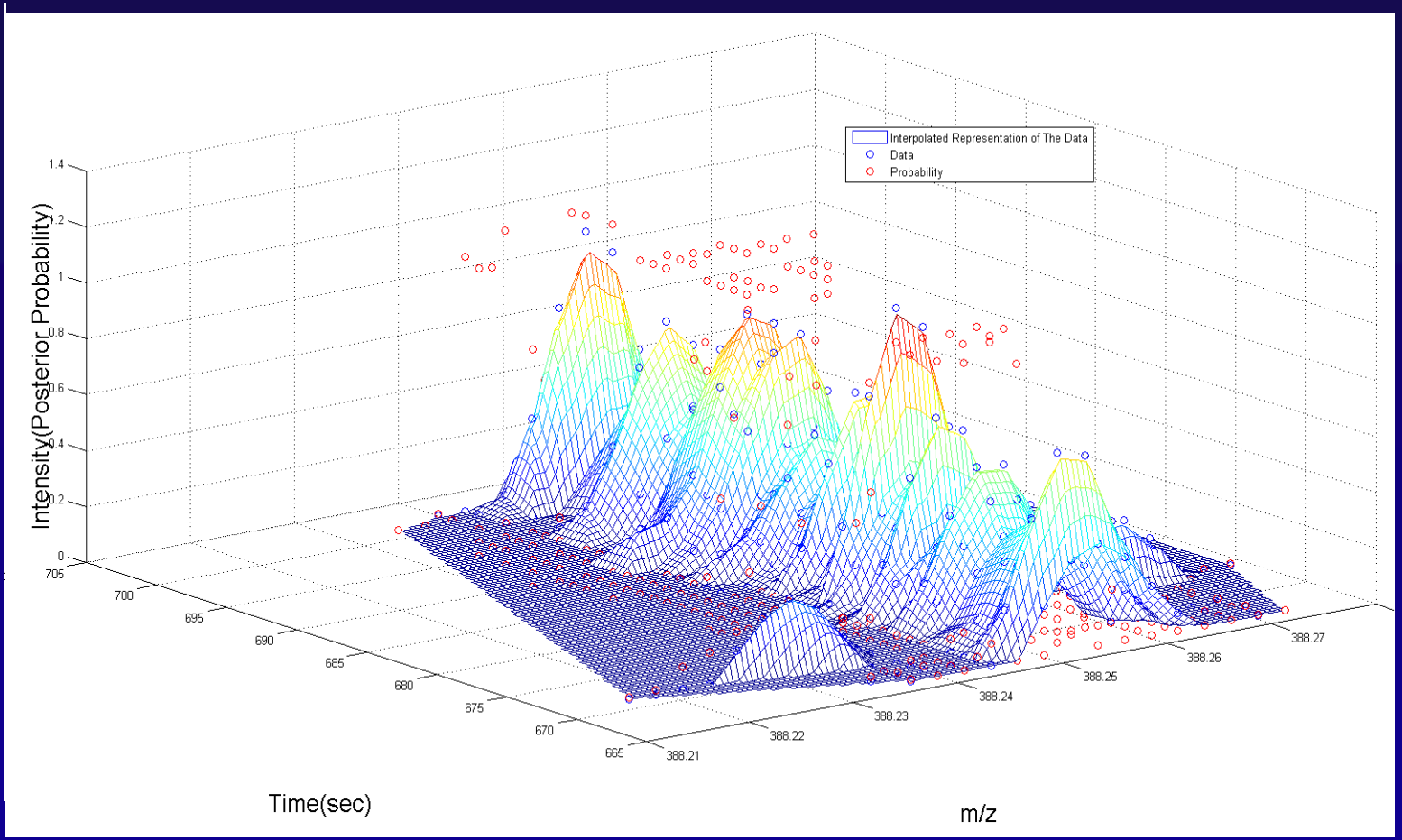
Example I



M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS. Results

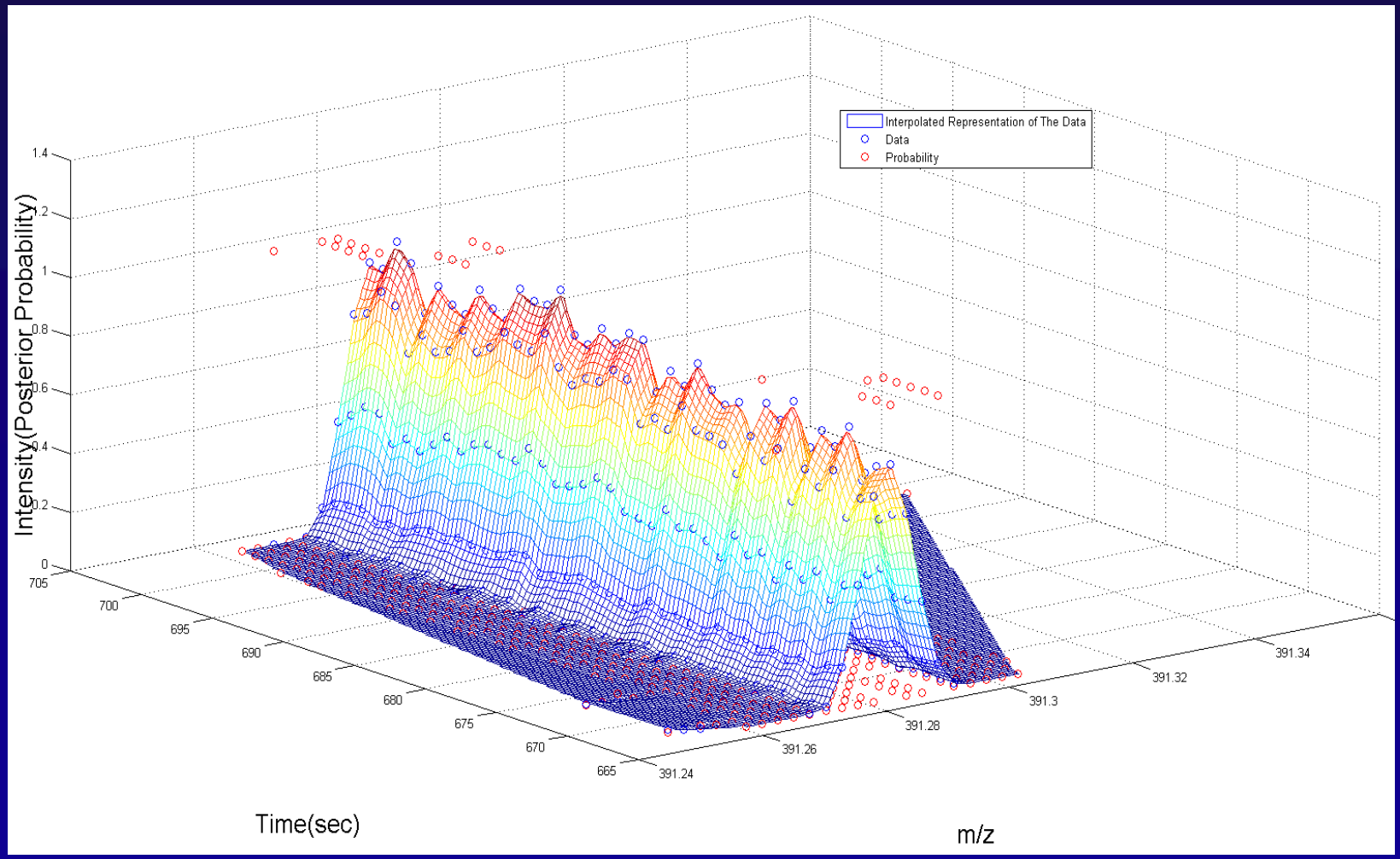
Example I



M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example I: peak detection in LC-MS. Results

Example I



M. Woldegebriel, G. Vivó-Truyols, Anal. Chem., accepted for publication

Example II: Targeted screening

In forensic toxicology, we want to know the probability of a compound (out of a list of ~500) being present (so we should submit the sample for confirmation)

What is the probability that the peak feature of a certain compound is present? ????

The peak feature is present H_1

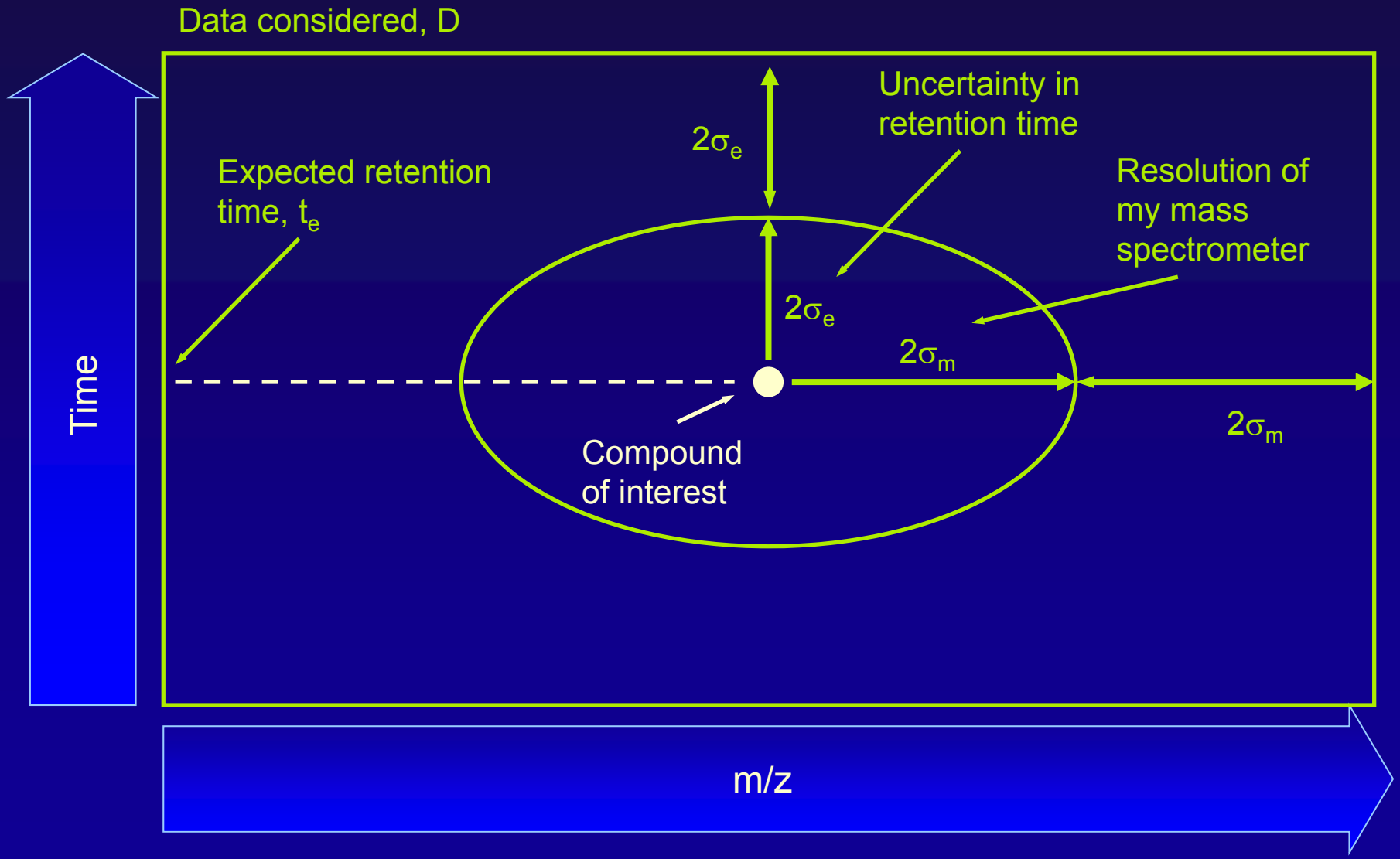
The peak feature is not present H_2

Posterior odds = Likelihood ratio x Prior odds

$$\frac{p(H_1|\mathrm{D})}{p(H_2|\mathrm{D})} = \frac{p(\mathrm{D}|H_1)}{p(\mathrm{D}|H_2)} \times \frac{p(H_1)}{p(H_2)}$$

Example II: Targeted screening

Example II



Example II: Targeted screening

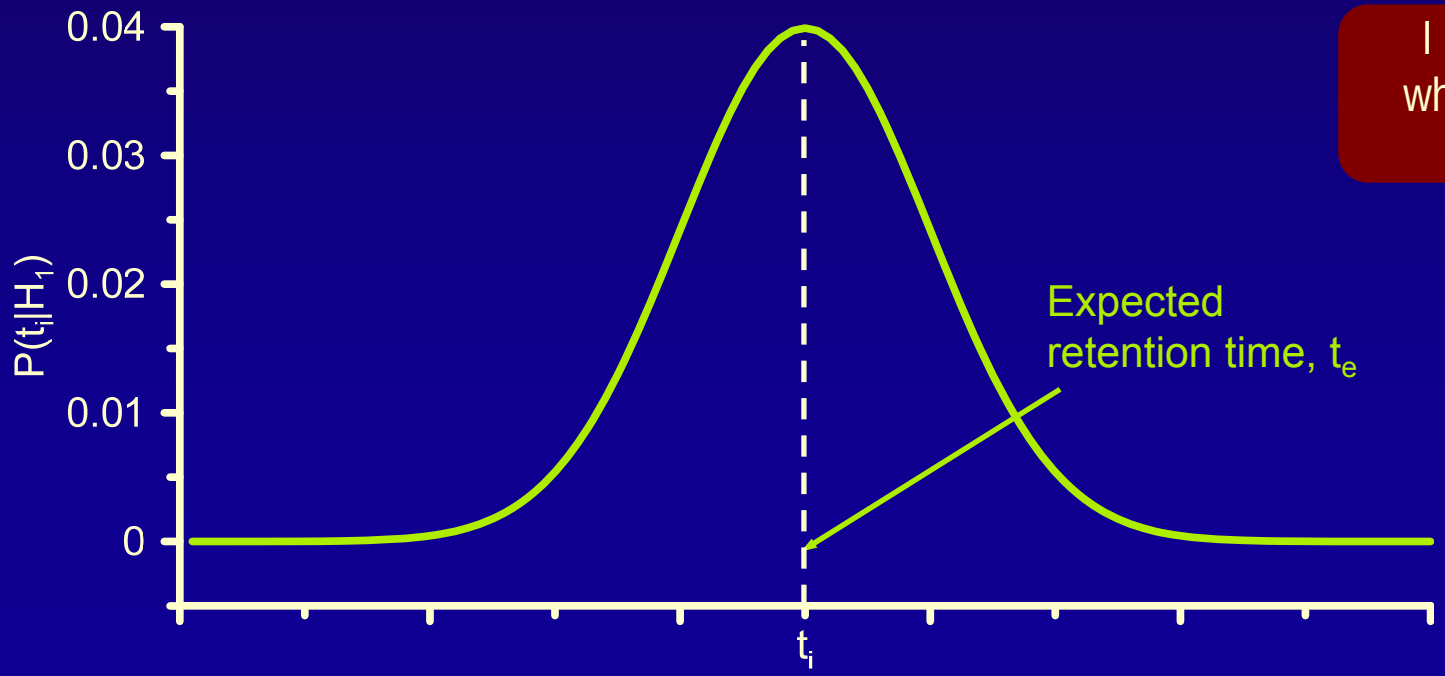
Example II

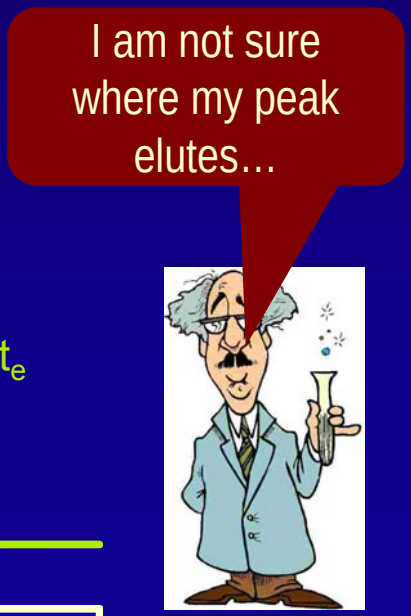
$$p(\mathrm{D}|H_1) = \sum_{i=1}^{k} \sum_{\mathrm{w}\in \mathrm{H}_1} \mathrm{P}(D|\mathrm{w}, t_i, \mathrm{H}_1)\, \mathrm{P}(\mathrm{w}|\mathrm{H}_1)\, \mathrm{P}(t_i|\mathrm{H}_1)$$

Model case (excluding change in t_R)

My peak can elute at various t_i values

What is the prior probability distribution for the elution time?





Example II: Targeted screening

Example II

Evidence D_1 … *data at the most abundant isotope*

Posterior odds = Likelihood ratio x Prior odds

$$\frac{p(H_1|D_1)}{p(H_2|D_1)} = \frac{p(D_1|H_1)}{p(D_1|H_2)} \times \frac{p(H_1)}{p(H_2)}$$

Evidence D_2 … *isotope ratios*

Posterior odds = Likelihood ratio x Prior odds

$$\frac{p(H_1|D_1, D_2)}{p(H_2|D_1, D_2)} = \frac{p(D_2|H_1, D_1)}{p(D_2|H_2, D_1)} \times \frac{p(H_1|D_1)}{p(H_2|D_1)}$$

Example II: Targeted screening

Testing the method with 500 compounds

Bayesian vs. frequentist are not comparable!

We set up a threshold on the posterior probability to "declare" a match…

… and then we can compare with existing software

Bayesian screening

Sensitivity: 96.5%
Specificity 95.8%

Mass Hunter

Sensitivity: 93.5%
Specificity 95.5%

Example II: Targeted screening

Example II

In forensic toxicology, we want to know the probability of a compound (out of a list of ~500) being present (so we should submit the sample for confirmation)

What is the probability that the peak feature of a certain compound is present?

compound

The peak feature is present → H_1

compound

The peak feature is not present → H_2

Posterior odds = Likelihood ratio x Prior odds

$$\frac{p(H_1|\mathrm{D})}{p(H_2|\mathrm{D})} = \frac{p(\mathrm{D}|H_1)}{p(\mathrm{D}|H_2)} \times \frac{p(H_1)}{p(H_2)}$$

Conclusions

- Automation: the data-analysis part doesn't involve a decision → It is just informing the scientist about the probabilities of the different hypothesis being true…
- Weight the data, do not discard anything!.
- The good (old) theories work!: e.g. Statistical Overlap Theory (Davies, Giddings)
- Toxicology screening (including MS). Combining evidence: e.g. different number of isotopes, as well as uncertainty in the retention time.
- Bayesian screening gives probabilities (not decisions). When we convert it into a decision… we are beating the "Mass Hunter" software (Agilent).

Acknowledgements

Special thanks to...

- Analytical-chemistry group (University of Amsterdam).
- M. Sjerps (dept. of mathematics, univesrity of Amsterdam).
- COAST consortium (NWO + DSM + NFI + Rikilt) for funding.

Both the tutorial (Monday) and this presentation available at www.tecnometrix.com

Feel free to download and provide me feedback!

Thanks for your attention!