

Selectivity.
Confirmation of identity.

Introduction – selectivity

- Any analytical method must produce analytical signal in response to the presence of analyte in the sample.
- The signal should be unaffected by other substances in the sample.
- The extent to which this condition is met is termed **selectivity**.

Introduction – identity confirmation

- When an analytical signal is registered from the sample, it must be proved that the signal is due to analyte – **confirmation of identity**.
- Information required for identity confirmation is collected during validation.

LC-MS is one of the most selective analytical techniques, which also enables identity confirmation.

Selectivity

- IUPAC definition of selectivity:

The **extent** to which other substances interfere with the determination of a substance according to a given procedure.

- **Specificity** – 100% selectivity.

Selectivity terms in validation guidelines

„Selectivity“	„Specificity“
AOAC	ICH
EMA	NordVal
Eurachem	
FDA	
IUPAC	

Selectivity

- IUPAC definition of selectivity:

The extent to which other substances **interfere** with the determination of a substance according to a given procedure.

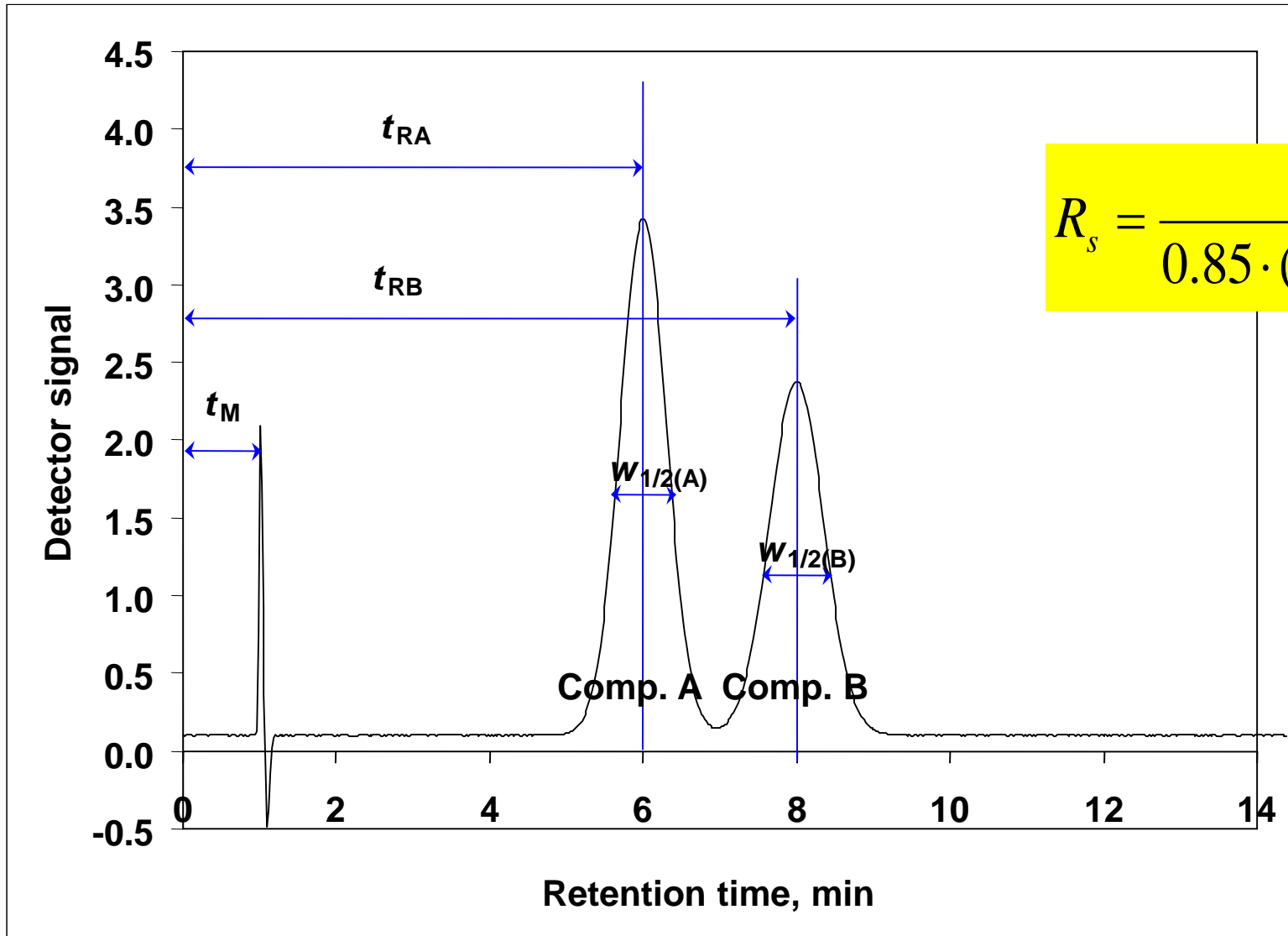
- **Interference** ...
 - substance behaves like analyte.
 - interferes with analytical signal (matrix effect).

Selectivity in LC-MS

- Selectivity arises from both:
 - LC separation process.
 - MS detection.

LC selectivity

Peak resolution



$$R_s = \frac{t_{RB} - t_{RA}}{0.85 \cdot (W_{1/2B} + W_{1/2A})}$$

Required LC selectivity

- Selectivity in terms of peak resolution:
 - FDA: $R_s \geq 2$
 - AOAC: $R_s \geq 1.5$
- Eurachem: demonstrate separation on different column.
- AOAC and ICH: no other compound should be detectable at analyte retention time when other methods (like IR, NMR and MS) are used.

Why are the requirements so different?

- Pharmaceutical analysis.
 - In active pharmaceutical ingredient (API) all synthesis by-products, degradants and additives may cause side-effects on patients.
 - Therefore each component of the sample appears as an analyte and must be chromatographically separated.
- Pesticide residue analysis in vegetables.
 - Vegetable extract is rich in compounds, which may co-elute with analyte.
 - Analysis results can still be adequate, if **detector** is only responsive to analyte and not matrix components.