Technische Universität Braunschweig

Wätzig et al.
Institut für Medizinische und Pharmazeutische Chemie

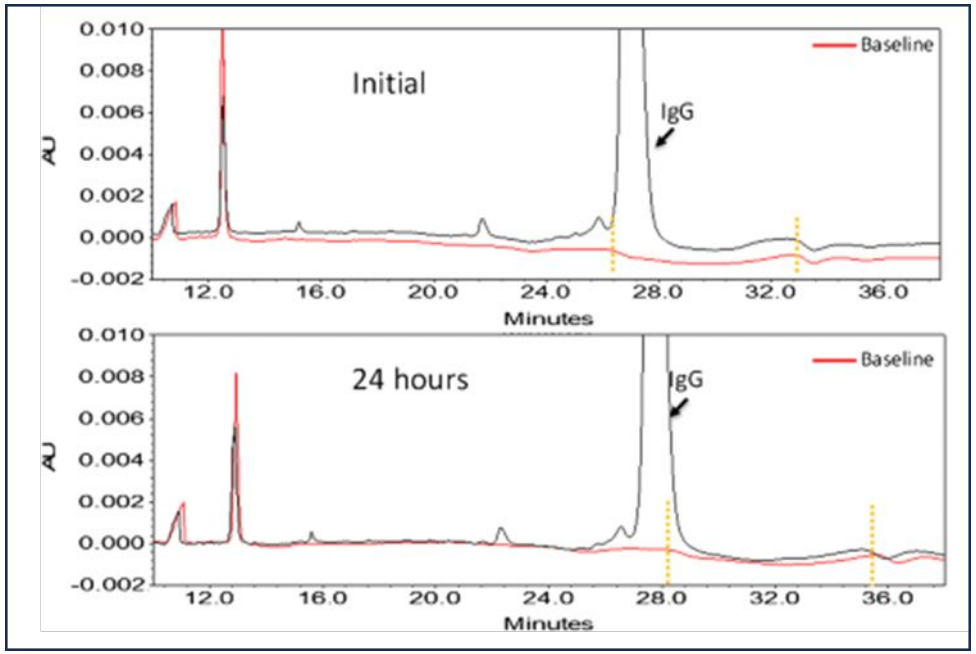
Integration of Electropherograms in GMP Labs Under Increasing Scrutiny Due to Data Integrity Intensive Inspections

Tim Blanc[1], Hermann Wätzig[2], Cari Sänger-van de Griend[2, 3, 4]

[1]*Eli Lilly and Company*
[2]*Institute of Medicinal and Pharmaceutical Chemistry, University of Braunschweig, Germany*
[3]*Kantisto BV, The Netherlands*
[4]*Department of Medicinal Chemistry, Faculty of Pharmacy, Uppsala Universitet, Sweden*

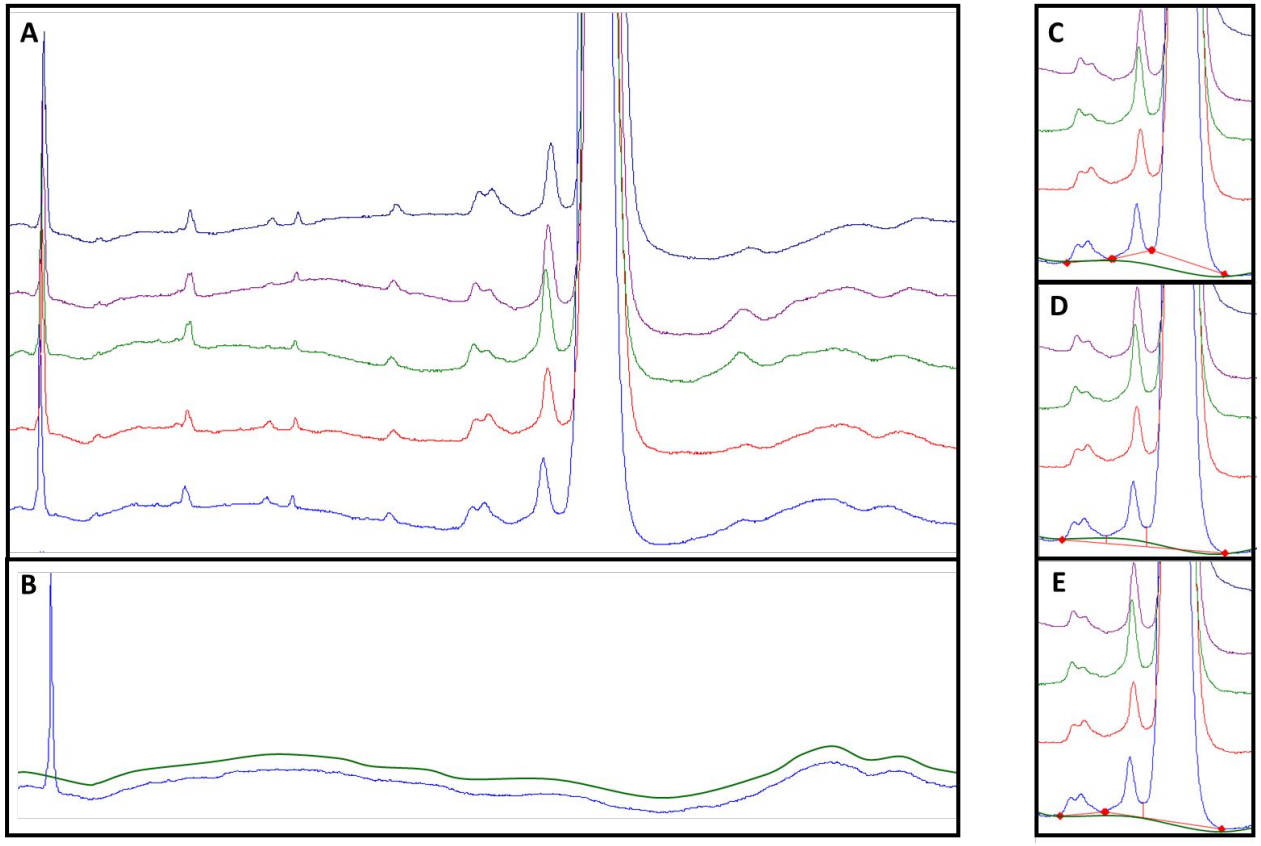
Correspondence: h.waetzig@tu-braunschweig.de

Peak integration: to get you into the mood



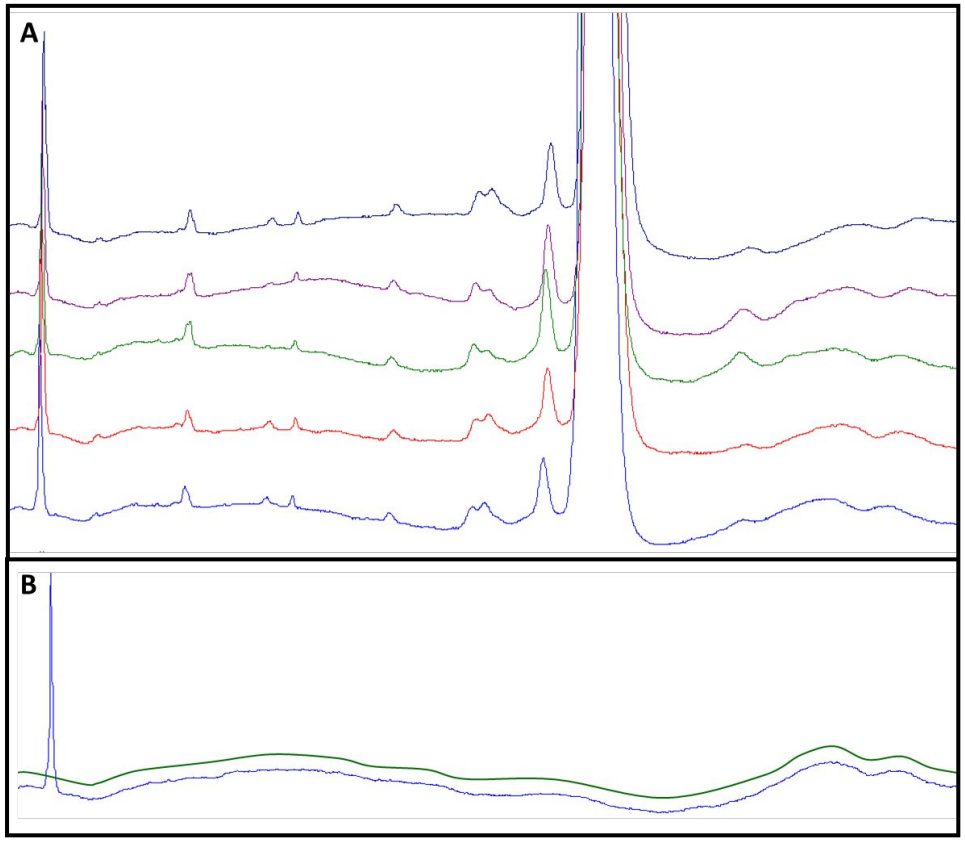
Systematic drift and quantification inconsistency in a CE-SDS non-reducing assay. Electropherograms of IgG drug overlaid with the corresponding baseline injected at the beginning (1 h, upper panel) and at the end (24 h, bottom panel) of a sample sequence. The IgG electropherogram (blank trace) should be the product of superimposition of the peak profiles and the baseline (red trace). A section of the baseline (highlighted by yellow dotted vertical lines) demonstrates the shift of the waviness.
[Gu Y, Voronov S, Ding J, Mussa N, Li ZJ. Assessment of CE-based baseline disturbances… . Analytical and Bioanalytical Chemistry. 2019;411(11):2425-37., used with permission].

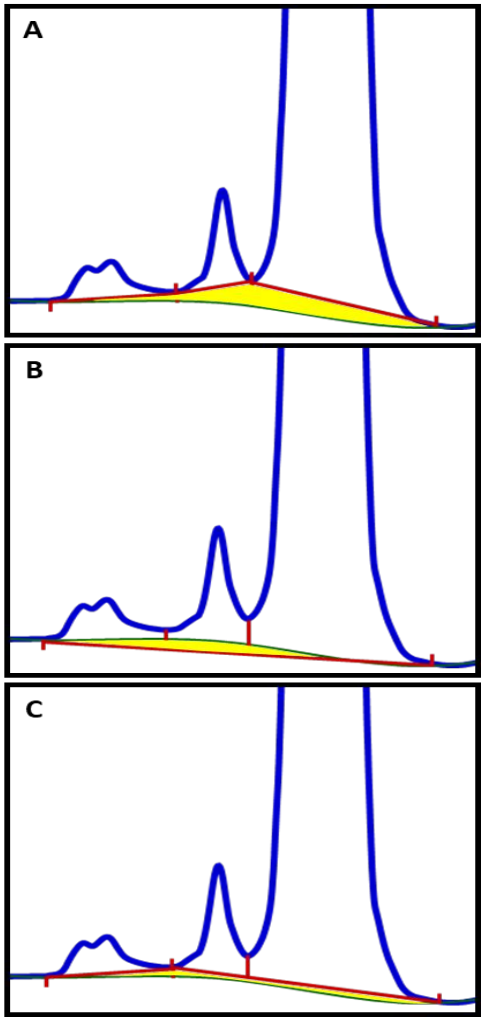
Peak integration: critical examples



Relationship between the baseline and sample electropherograms in CE-SDS. A: overlay of 5 sample electropherograms from a Non-Reduced CE-SDS assay. B: baseline. C “Valley-to-Valley” (red) approach D “Common Baseline” approach (spline) to integration. E: hybrid approach, provides the integration closest to the blank baseline

Peak integration: critical examples

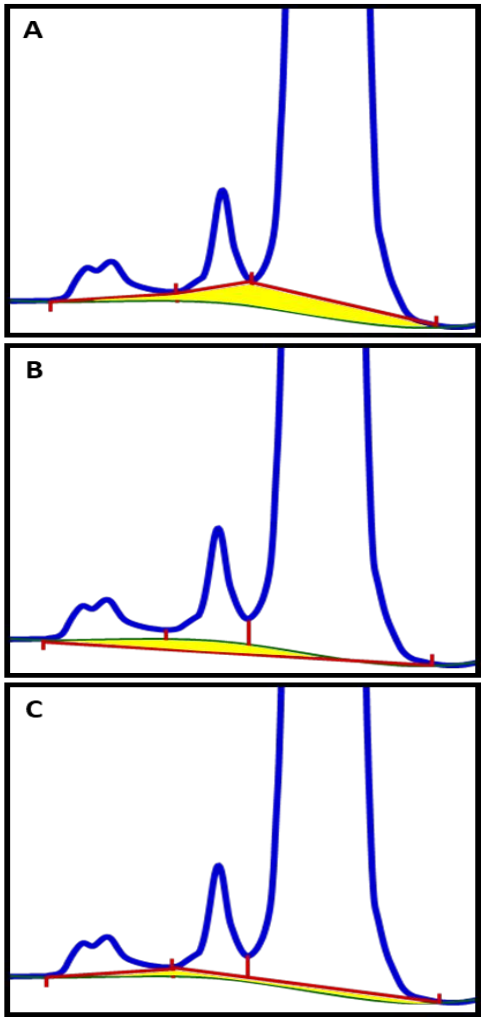




Peak integration: critical examples

Tim Blanc

Cari Sänger



Peak integration, sources: a selection
[for a more detailed list can be found in Blanc, Wätzig, Sänger 2024]

FDA's guidance document "Data integrity and Compliance with Drug CGMP: Questions and Answers"

USP, Ph.Eur. and JP

WHO: "TRS 1033 - Annex 4: WHO Guideline on data integrity"

Technical Report 80: Data Integrity Management System for Pharmaceutical Laboratories (Parenteral Drug Association [PDA], Bethesda, Maryland, 2018)

McDowall R., e.g: Are you controlling peak integration to ensure data integrity? LCGC North America. 2020;38(6):346–54-–54.

Snyder LR, Kirkland JJ, Dolan JW.: Introduction to modern liquid chromatography John Wiley & Sons; 2011.

Dyson NA. Chromatographic integration methods Royal Society of Chemistry; 1998.

Peak integration

- Integration in GMP laboratories is critically important
  - has become focus of data integrity-centric regulatory inspections

- Data systems developed for chromatograms rather than electropherograms, and the increased regulatory scrutiny call for a resolution.

- This extends to R&D, clinical, and academic labs

Tim Blanc, Hermann Wätzig and Cari Sänger, in preparation

Peak integration, sources: a selection

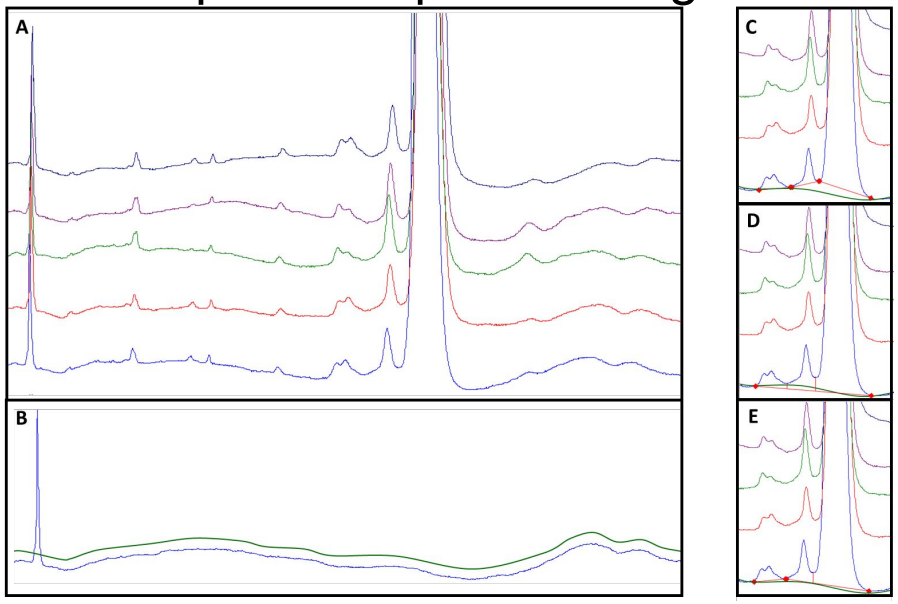
[for a more detailed list can be found in Blanc, Wätzig, Sänger 2024]

- Never wrong, but often very general
- CE ≠ LC
- CE can pose unique challenges

Peak integration, sources: a selection

[for a more detailed list can be found in Blanc, Wätzig, Sänger 2024]

- Never wrong, but often very general
- CE ≠ LC
- CE can pose unique challenges



Peak integration: what do we need?

- Analytical Procedures
- CE-specific solutions
- Standard Operation Procedures
- Training

Peak integration: Analytical Procedures / SOPs

- Details!
- Examples/illustrations!

List of relevant CE parameters

Table 19. *Experimental parameters to define method*

- Buffer: pH, molarity; recipe: weight or volume of all chemicals used
- Sample solvent
- Separation: pole outlet, U, I
- Capillary: material, ID, l, L
- Injection: t, $U/\Delta p$
- Detection: wavelength, instrumentation
- Temperature
- Rinsing procedures (t, reagents, Δp); equilibration times
- Shelf time of solutions, if relevant

Strategies for method development and validation in CE - related to pharmaceutical and biological applications

Hermann Wätzig, Matthias Degenhardt, Annette Kunkel

Electrophoresis 1998;19:2695–752.

Strategies for capillary electrophoresis: Method development and validation for pharmaceutical and biological applications – updated and completely revised edition

Electrophoresis 2023; DOI: 10.1002/elps.202300158

Finja Krebs[1], Holger Zagst[1], Matthias Stein[1], Ratih Ratih[2], Robert Minkner[1], Mais Olabi[1], Sophie Hartung[1], Christin Scheller[1], Blanca H. Lapizco-Encinas[3*], Cari Sänger-van de Griend[4,5*], Carlos D. García[6*], Hermann Wätzig[1*]

Strategies for capillary electrophoresis: Method development and validation for pharmaceutical and biological applications – updated and completely revised edition

Finja Krebs[1], Holger Zagst[1], Matthias Stein[1], Ratih Ratih[2], Robert Minkner[1], Mais Olabi[1], Sophie Hartung[1], Christin Scheller[1], Blanca H. Lapizco-Encinas[3*], Cari Sänger-van de Griend[4,5*], Carlos D. García[6*], Hermann Wätzig[1*]

Electrophoresis 2023; DOI: 10.1002/elps.202300158

Strategies for method development and validation in CE - related to pharmaceutical and biological applications

Hermann Wätzig, Matthias Degenhardt, Annette Kunkel

Electrophoresis 1998;19:2695–752.

Strategies for capillary electrophoresis: Method development and validation for pharmaceutical and biological applications – updated and completely revised edition

Electrophoresis 2023; DOI: 10.1002/elps.202300158

TABLE 8 Two established methods for capillary zone electrophoresis (CZE) of monoclonal antibodies (mAbs): method and performance parameters.

(I) T-EthA method for the concentration determination of mAb (in example process samples) [193]

Polyvinyl alcohol (PVA)-coated capillaries with 50-µm id, a total length of 33 cm with an effective length of 24.5 or 8.5 cm (e.g., Agilent Technologies)

Separation voltage: 16 kV, ramped over 0.5 min (approx. 45 µA)

Sample injection at 10 mbar for 5 s, followed by the injection of a BGE plug using the same conditions

$T = 20°C$

$\lambda = 210$ nm

Conditioning: PVA capillary successively flushed with 10 mM phosphoric acid, water, and BGE at 1 bar for 20 min each before first used, and for 10 min each at beginning of each working day. Before injection, capillary flushed with 10 mM phosphoric acid for 1 min and BGE for 2 min, each at 1 bar

BGE: 100 mM phosphoric acid, 70 mM T-EthA, 0.1% poloxamer. pH after preparation: 2.5

The intra-day precision and accuracy were 2%–12% and 88%–107%, respectively, and inter-day precision and accuracy were 4%–9% and 93%–104%, respectively

t_{ana} = 6–11 min

(II) eACA method for the charge heterogeneity determination in drug substance and drug product [170]

The BGE comprising 400 mM eACA and 2.0 mM. The different reasons for peak broadening are longitudinal diffusion, Joule heating, the influence of sample plug length, the influence of the EOF, the effect of electromigration dispersion protein, and adsorption to the capillary wall TETA adjusted to pH 5.7 with glacial acetic acid, and 0.05% HPMC was used. First, 420 mM eACA, and 2.1 mM TETA at pH 5.7 was prepared, which can be stored at 2–8°C with an expiration date of 6 months. Add 13.8 g of eACA and approximately 170.0 mL of deionized water to a 250-mL glass beaker and stir until dissolved. Add 76.8 µL of TETA and stir to mix the solution. Adjust pH to 5.7 ± 0.05 with glacial acetic acid. Transfer the solution to a 250-mL glass volumetric flask and fill to 250.0-mL volume with deionized water. Afterward, the 1% (w/v) HPMC was prepared which can be stored at ambient temperature with an expiry date of 3 months. A volume of 30.0-mL deionized water was added to a 50-mL glass volumetric flask followed by 0.3 g of HPMC slowly added to help disperse HPMC. Stir covered overnight or until dissolved at ambient temperature. Both solutions (19.0 mL of 420 mM eACA 2.1 mM TETA buffer [pH 5.7] and 1.0 mL of 1% HPMC into a 20-mL glass volumetric flask) were combined to reach the final concentration of the BGE. The BGE can be used for 2 weeks and needs to be stored at 5°C in the refrigerator. For capillary storage, 10 mM phosphoric acid, for the rinsing procedure, 0.1 M hydrochloric acid was used.

There are *two versions* of the method that differ in capillary lengths and separation voltages:

High speed with a capillary of 10 cm (Sciex)/8.5 cm (Agilent) effective length, and of 30 cm (Sciex)/33 cm (Agilent) total length, and a separation voltage of 29 kV (Sciex)/30 kV (Agilent), as well as, *high resolution* with a capillary of 40 cm (Sciex, and Agilent) effective length, and of 50 cm (Sciex)/48.5 cm (Agilent) total length, and 20 kV (Sciex)/19.4 kV (Agilent)

$\Lambda = 214$ nm, 8 Hz (Sciex)/10 Hz (Agilent)

$T = 25°C$ (separation); $T = 15°C$ (sample storage)

Sample injection by applying 35 mbar (0.5 psi) for 5 s for high speed and for 10 s for high resolution.

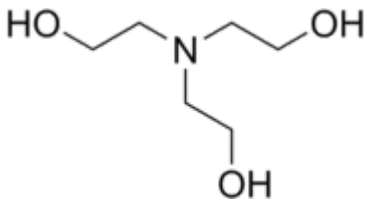
More method details can be found in Wiesner et al. (in press) and the corresponding supplementary material (Tables S2–S4).

%Corrected peak area: 0.2%–2% RSD

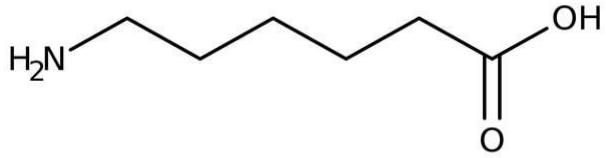
t_{ana} = 2.5–4 min (high speed), 20–35 min (high resolution)

Abbreviations: BGE, background electrolyte; eACA, ε-aminocaproic acid; HPMC, hydroxypropyl methylcellulose; PVA, polyvinyl alcohol; T-EthA, triethanolamine.

T-EthA method(s)



eACA method(s)



Protein methods

List of relevant CE parameters

Table 19. *Experimental parameters to define method*

- Buffer: pH, molarity; recipe: weight or volume of all chemicals used
- Sample solvent
- Separation: pole outlet, U, I
- Capillary: material, ID, l, L
- Injection: t, $U/\Delta p$
- Detection: wavelength, instrumentation
- Temperature
- Rinsing procedures (t, reagents, Δp); equilibration times
- Shelf time of solutions, if relevant

Strategies for method development and validation in CE - related to pharmaceutical and biological applications

Hermann Wätzig, Matthias Degenhardt, Annette Kunkel

Electrophoresis 1998;19:2695–752.

List of relevant integration parameters according to various Chromatography Data Systems (CDS)

Timed Integration Events	ChemStation	Chromeleon	Empower	32 Karat
Core integration Functions	Slope Sensitivity	Sensitivity	Liftoff	Threshold
			Touchdown	
	Peak Width	Peak Slice	Peak Width	Width
	Auto Peak Width			
	Area Reject	Minimum Area	Minimum Area	Minimum Area
			Maximum Area	
	Height Reject	Minimum Height	Minimum Height	
			Maximum Height	
Integration functions for unresolved peaks	Shoulders Peak	Shoulder Threshold	Detect Shoulders	Shoulder Sensitivity
	Detect Shoulders			
	Shoulder Mode			
	Split Peak -		Force Drop Line	Split PEak
	Tail Tangent Skim -		Exponential Skim	Back Tangent Skim Front Tangent Skim
	Tangent Skim Mode -		Tangential Skim	
	Baseline at Valleys	Valley to Valley	Valley to Valley	Valley to Valley
Integration functions for baseline corrections	Baseline Now	Lock Baseline		Move Baseline Start
	Baseline Hold	Lock Baseline		Move Baseline Stop
	Baseline Backwards -		Forward Horizontal	Horizontal Baseline
	Baseline Next Valley -		Reverse Horizontal	Backward Horizontal Baseline
			Force Baseline	Manual Baseline
			Force Peak	Manual Peak
Miscellaneous Integration functions	Integration	Inhibit Integration	Inhibit Integration	Integration Off
	Area Sum	Peak Group Start		Define Group
	Peak Group End			Define Group
	Solvent Peak -			
	Negative Peak	Detect Negative Peaks	Allow Negative Peaks	Negative Peak
Advanced Peak Detection Algorithms	Peak Recognition Filters	Cobra	Apex Track	Ceasar Integration

Tim Blanc

Cari Sänger

List of relevant integration parameters according to various Chromatography Data Systems (CDS)

Timed Integration Events	ChemStation	Chromeleon	Empower	32 Karat
Core integration Functions	Slope Sensitivity	Sensitivity	Liftoff	Threshold
			Touchdown	
	Peak Width	Peak Slice	Peak Width	Width
	Auto Peak Width			
	Area Reject	Minimum Area	Minimum Area	Minimum Area
			Maximum Area	
	Height Reject	Minimum Height	Minimum Height	
			Maximum Height	
Integration functions for unresolved peaks	Shoulders Peak	Shoulder Threshold	Detect Shoulders	Shoulder Sensitivity
	Detect Shoulders			
	Shoulder Mode			
	Split Peak -		Force Drop Line	Split PEak
	Tail Tangent Skim -		Exponential Skim	Back Tangent Skim Front Tangent Skim
	Tangent Skim Mode -		Tangential Skim	
	Baseline at Valleys	Valley to Valley	Valley to Valley	Valley to Valley
Integration functions for baseline corrections	Baseline Now	Lock Baseline		Move Baseline Start
	Baseline Hold	Lock Baseline		Move Baseline Stop
	Baseline Backwards -		Forward Horizontal	Horizontal Baseline
	Baseline Next Valley -		Reverse Horizontal	Backward Horizontal Baseline
			Force Baseline	Manual Baseline
			Force Peak	Manual Peak
Miscellaneous Integration functions	Integration	Inhibit Integration	Inhibit Integration	Integration Off
	Area Sum	Peak Group Start		Define Group
	Peak Group End			Define Group
	Solvent Peak -			
	Negative Peak	Detect Negative Peaks	Allow Negative Peaks	Negative Peak
Advanced Peak Detection Algorithms	Peak Recognition Filters	Cobra	Apex Track	Ceasar Integration

Tim Blanc

Cari Sänger

List of relevant integration parameters according to various Chromatography Data Systems (CDS)

Timed Integration Events	ChemStation	Chromeleon	Empower	32 Karat
Core integration Functions	Slope Sensitivity	Sensitivity	Liftoff	Threshold
			Touchdown	
	Peak Width	Peak Slice	Peak Width	Width
	Auto Peak Width			
	Area Reject	Minimum Area	Minimum Area	Minimum Area
			Maximum Area	
	Height Reject	Minimum Height	Minimum Height	
			Maximum Height	
Integration functions for unresolved peaks	Shoulders Peak	Shoulder Threshold	Detect Shoulders	Shoulder Sensitivity
	Detect Shoulders			
	Shoulder Mode			
	Split Peak -		Force Drop Line	Split PEak
	Tail Tangent Skim -		Exponential Skim	Back Tangent Skim Front Tangent Skim
	Tangent Skim Mode -		Tangential Skim	
	Baseline at Valleys	Valley to Valley	Valley to Valley	Valley to Valley
Integration functions for baseline corrections	Baseline Now	Lock Baseline		Move Baseline Start
	Baseline Hold	Lock Baseline		Move Baseline Stop
	Baseline Backwards -		Forward Horizontal	Horizontal Baseline
	Baseline Next Valley -		Reverse Horizontal	Backward Horizontal Baseline
			Force Baseline	Manual Baseline
			Force Peak	Manual Peak
Miscellaneous Integration functions	Integration	Inhibit Integration	Inhibit Integration	Integration Off
	Area Sum	Peak Group Start		Define Group
	Peak Group End			Define Group
	Solvent Peak -			
	Negative Peak	Detect Negative Peaks	Allow Negative Peaks	Negative Peak
Advanced Peak Detection Algorithms	Peak Recognition Filters	Cobra	Apex Track	Ceasar Integration

Timed Integration Events	ChemStation	Chromeleon	Empower	32 Karat
Core integration Functions	Slope Sensitivity	Sensitivity	Liftoff	Threshold
			Touchdown	
	Peak Width	Peak Slice	Peak Width	Width
	Auto Peak Width			
	Area Reject	Minimum Area	Minimum Area	Minimum Area
			Maximum Area	
	Height Reject	Minimum Height	Minimum Height	
			Maximum Height	
Integration functions for unresolved peaks	Shoulders Peak	Shoulder Threshold	Detect Shoulders	Shoulder Sensitivity
	Detect Shoulders			
	Shoulder Mode			
	Split Peak -		Force Drop Line	Split PEak
	Tail Tangent Skim -		Exponential Skim	Back Tangent Skim Front Tangent Skim
	Tangent Skim Mode -		Tangential Skim	
	Baseline at Valleys	Valley to Valley	Valley to Valley	Valley to Valley

List of relevant integration parameters according to various Chromatography Data Systems (CDS)

Timed Integration Events	ChemStation	Chromeleon	Empower	32 Karat
Core integration Functions	Slope Sensitivity	Sensitivity	Liftoff	Threshold
			Touchdown	
	Peak Width	Peak Slice	Peak Width	Width
	Auto Peak Width			
	Area Reject	Minimum Area	Minimum Area	Minimum Area
			Maximum Area	
	Height Reject	Minimum Height	Minimum Height	
			Maximum Height	
Integration functions for unresolved peaks	Shoulders Peak	Shoulder Threshold	Detect Shoulders	Shoulder Sensitivity
	Detect Shoulders			
	Shoulder Mode			
	Split Peak -		Force Drop Line	Split PEak
	Tail Tangent Skim -		Exponential Skim	Back Tangent Skim Front Tangent Skim
	Tangent Skim Mode -		Tangential Skim	
	Baseline at Valleys	Valley to Valley	Valley to Valley	Valley to Valley
Integration functions for baseline corrections	Baseline Now	Lock Baseline		Move Baseline Start
	Baseline Hold	Lock Baseline		Move Baseline Stop
	Baseline Backwards -		Forward Horizontal	Horizontal Baseline
	Baseline Next Valley -		Reverse Horizontal	Backward Horizontal Baseline
			Force Baseline	Manual Baseline
			Force Peak	Manual Peak
Miscellaneous Integration functions	Integration	Inhibit Integration	Inhibit Integration	Integration Off
	Area Sum	Peak Group Start		Define Group
	Peak Group End			Define Group
	Solvent Peak -			
	Negative Peak	Detect Negative Peaks	Allow Negative Peaks	Negative Peak
Advanced Peak Detection Algorithms	Peak Recognition Filters	Cobra	Apex Track	Ceasar Integration

Timed Integration Events	ChemStation	Chromeleon	Empower	32 Karat
Core integration Functions	Slope Sensitivity	Sensitivity	Liftoff	Threshold
			Touchdown	
	Peak Width	Peak Slice	Peak Width	Width
	Auto Peak Width			
	Area Reject	Minimum Area	Minimum Area	Minimum Area
			Maximum Area	
	Height Reject	Minimum Height	Minimum Height	
			Maximum Height	
Integration functions for unresolved peaks	Shoulders Peak	Shoulder Threshold	Detect Shoulders	Shoulder Sensitivity
	Detect Shoulders			
	Shoulder Mode			
	Split Peak -		Force Drop Line	Split Peak
	Tail Tangent Skim -		Exponential Skim	Back Tangent Skim Front Tangent Skim
	Tangent Skim Mode -		Tangential Skim	
	Baseline at Valleys	Valley to Valley	Valley to Valley	Valley to Valley

List of relevant integration parameters according to various Chromatography Data Systems (CDS)

Timed Integration Events	ChemStation	Chromeleon	Empower	32 Karat
Core integration Functions	Slope Sensitivity	Sensitivity	Liftoff	Threshold
			Touchdown	
	Peak Width	Peak Slice	Peak Width	Width
	Auto Peak Width			
	Area Reject	Minimum Area	Minimum Area	Minimum Area
			Maximum Area	
	Height Reject	Minimum Height	Minimum Height	
			Maximum Height	
Integration functions for unresolved peaks	Shoulders Peak	Shoulder Threshold	Detect Shoulders	Shoulder Sensitivity
	Detect Shoulders			
	Shoulder Mode			
	Split Peak -		Force Drop Line	Split PEak
	Tail Tangent Skim -		Exponential Skim	Back Tangent Skim Front Tangent Skim
	Tangent Skim Mode -		Tangential Skim	
	Baseline at Valleys	Valley to Valley	Valley to Valley	Valley to Valley
Integration functions for baseline corrections	Baseline Now	Lock Baseline		Move Baseline Start
	Baseline Hold	Lock Baseline		Move Baseline Stop
	Baseline Backwards -		Forward Horizontal	Horizontal Baseline
	Baseline Next Valley -		Reverse Horizontal	Backward Horizontal Baseline
			Force Baseline	Manual Baseline
			Force Peak	Manual Peak
Miscellaneous Integration functions	Integration	Inhibit Integration	Inhibit Integration	Integration Off
	Area Sum	Peak Group Start		Define Group
	Peak Group End			Define Group
	Solvent Peak -			
	Negative Peak	Detect Negative Peaks	Allow Negative Peaks	Negative Peak
Advanced Peak Detection Algorithms	Peak Recognition Filters	Cobra	Apex Track	Ceasar Integration

Integration functions for baseline corrections	Baseline Now	Lock Baseline		Move Baseline Start
	Baseline Hold	Lock Baseline		Move Baseline Stop
	Baseline Backwards -		Forward Horizontal	Horizontal Baseline
	Baseline Next Valley -		Reverse Horizontal	Backward Horizontal Baseline
			Force Baseline	Manual Baseline
			Force Peak	Manual Peak
Miscellaneous Integration functions	Integration	Inhibit Integration	Inhibit Integration	Integration Off
	Area Sum	Peak Group Start		Define Group
	Peak Group End			Define Group
	Solvent Peak -			
	Negative Peak	Detect Negative Peaks	Allow Negative Peaks	Negative Peak
Advanced Peak Detection Algorithms	Peak Recognition Filters	Cobra	Apex Track	Ceasar Integration

Peak integration: what do we need?

- Analytical Procedures
- Standard Operation Procedures
  - Example of integrated signal in method SOP
  - Initial integration settings in method SOP
  - Possibly: Indication that manual integration is allowed in method SOP
- Training

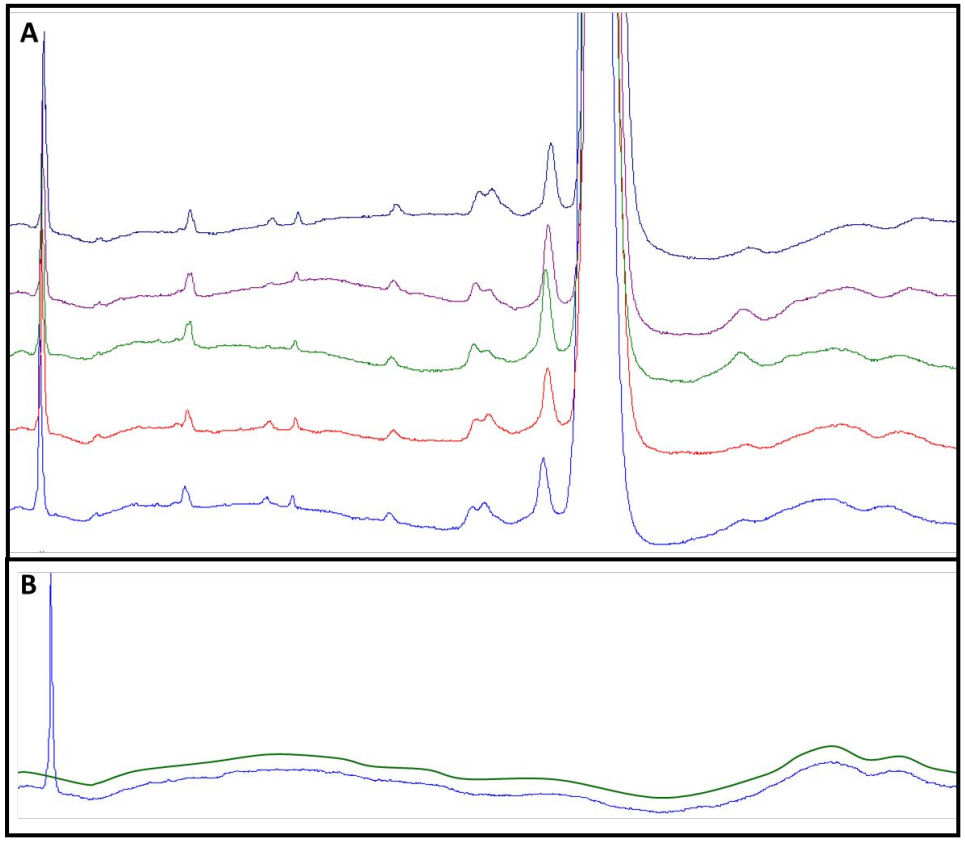
Peak integration: Auto-Integration!

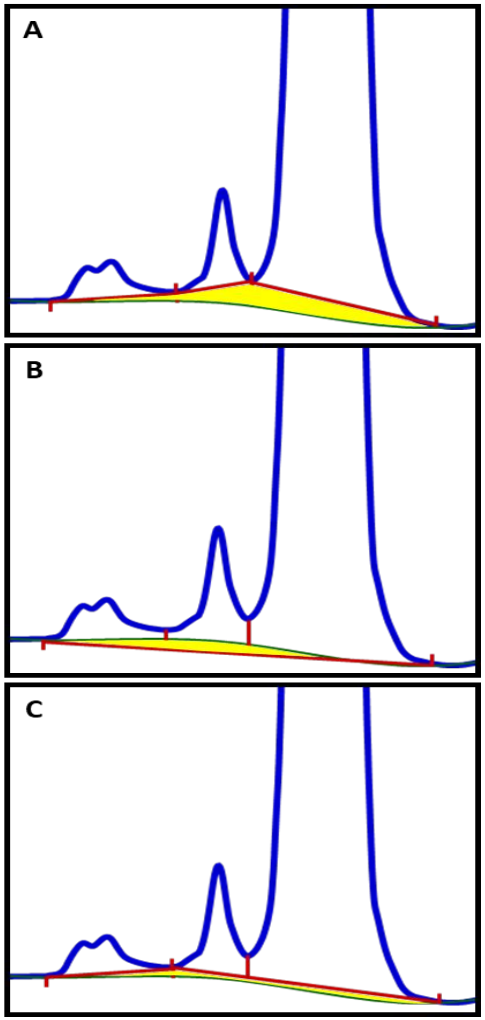
Peak integration: Auto-Integration! But also Manual Integration!

Peak integration: Auto-Integration! But also Manual Integration!

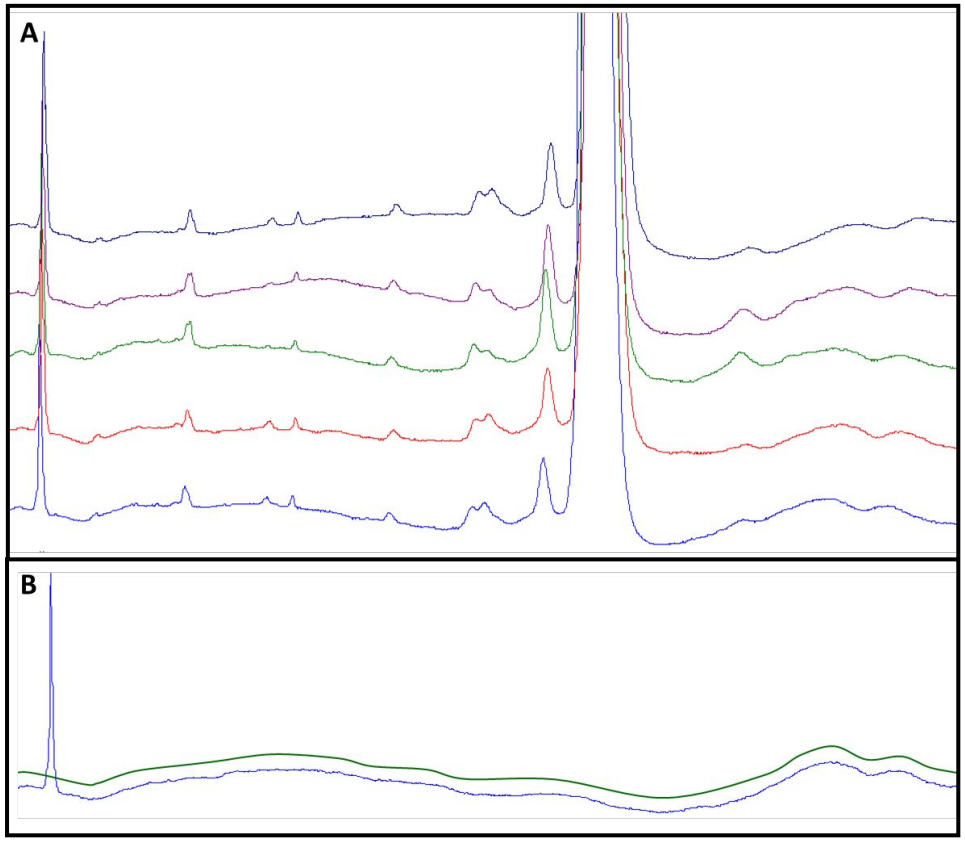
- Careful consideration necessary!
- Arbitrariness unacceptable
- but: auto-integration not always perfect. State-of-the-art needs improvements!
- Complex baselines must remain manageable
- Details!
- Examples/illustrations!

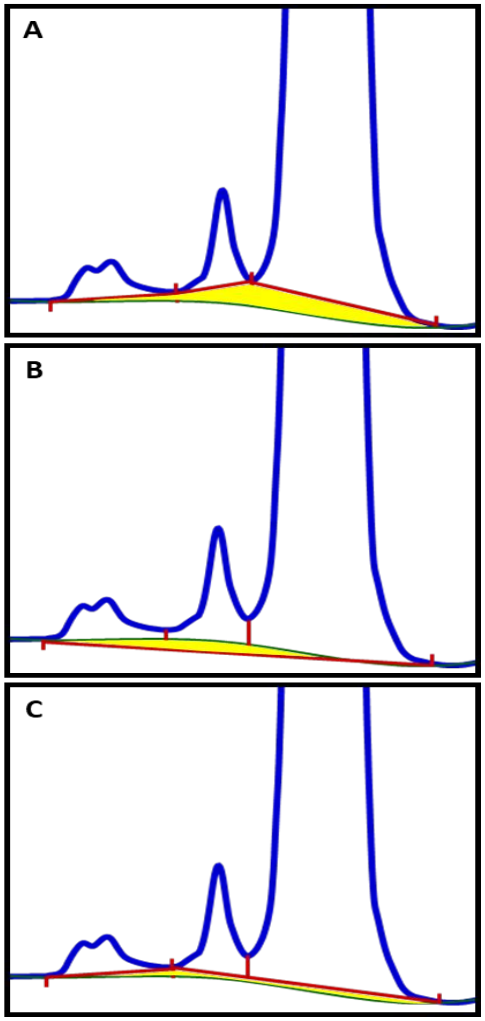
Manual Integration: Details! Examples, Illustrations!





Manual Integration: Details! Examples, Illustrations!





Raw data supplements, typical rates

Peak integration: Outlook

- Industry collaboration to create practical integration guidelines for CE

Peak integration: Outlook

- Industry collaboration to create practical integration guidelines for CE
  - Parameter list: discuss and complete
  - Examples for Good Integration Practices
  - Benchmark data sets with mutually agreed (“correct”) integration

Peak integration: Outlook

- Industry collaboration to create practical integration guidelines for CE
  - Parameter list: discuss and complete
  - Examples for Good Integration Practices
  - Benchmark data sets with mutually agreed (“correct”) integration
    - up to date, not too old, to show realistic data quality
    - curated collection, including QC and vendors data sets
      [data format?]

Peak integration: Outlook

- Industry collaboration to create practical integration guidelines for CE
  - Parameter list: discuss and complete
  - Examples for Good Integration Practices
  - Benchmark data sets with mutually agreed (“correct”) integration
    - up to date, not too old, to show realistic data quality
    - curated collection, including QC and vendors data sets
      [data format?]

- Improvement of auto-integration based on benchmark sets
  “enhanced” peak height (partial area), baseline description/models, splines and beyond, scaling x axes to µ, generalized peak models, filters

Peak integration: Conclusions

- We need Analytical Procedure (APs) and Standard Operating Procedures (SOPs)
- We need detailed method descriptions, defaults, parameter lists, illustrations, training
- We need to keep manual integration at the present time

Peak integration: Conclusions

- We need APs and SOPs
- We need detailed method descriptions, defaults, parameter lists, illustrations, training
- We need to keep manual integration at the present time
- Collaboration within the industry for generally accepted standards

Peak integration: Conclusions

- We need APs and SOPs
- We need detailed method descriptions, defaults, parameter lists, illustrations, training
- We need to keep manual integration at the present time
- Collaboration within the industry for generally accepted standards

Tim Blanc

Cari Sänger

Peak integration: Conclusions

- We need APs and SOPs
- We need detailed method descriptions, defaults, parameter lists, illustrations, training
- We need to keep manual integration at the present time
- Collaboration within the industry for generally accepted standards
- Benchmark data sets could be an important step
- Based on this, considerable improvements in integration algorithms are possible
- So probably less manual integration in the future, but at present it is still a must

Thank you very much!

Robert Minkner, Finja Krebs, Yannick Wilke, Hermann Wätzig, Holger Zagst, Mais Olabi, Marc Hoffstedt, Sophie Hartung

Peak integration: Conclusions

- We need APs and SOPs
- We need detailed method descriptions, defaults, parameter lists, illustrations, training
- We need to keep manual integration at the present time
- Collaboration within the industry for generally accepted standards
- Benchmark data sets could be an important step
- Based on this, considerable improvements in integration algorithms are possible
- So probably less manual integration in the future, but at present it is still a must