State of the art of size- and interaction based separations for industrial polymers

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International Symposium on GPC/SEC and related techniques
Amsterdam, September 27, 2016
Outline: the industrial perspective in analytical polymer separations

Introduction DSM, DSM-Resolve.

Some of our recent progresses and faced challenges in polymer separations:

- How to improve precision and how accurate can we get in industrial practice?
- Short-chain and long-chain branching in practice.
- Extremely high molar masses in SEC.
- Current status of APC.
- Current relevance of 2D-LC for polymers?
DSM: Building on an impressive history

- Hoffman La Roche’s Vitamins (1930s)
- Gist-Brocades (1869)
- DSM 1902

**Chemical synthesis & biotechnology**

**Life Sciences**
- Vitamins
- Omega’s
- Carotenoids
- Premixes for food & feed
- Enzymes
- Minerals
- Cultures & Yeasts
- Nutraceuticals
- Pharmaceuticals
- Cellulosic bioethanol
- Biomedical materials
- Bio-plastics
- High Performance Plastics
- Coating Resins
- Functional Materials
- Solar - advanced surfaces

**Materials Sciences**
- Energy, chemistry & polymer technology
100% DSM.

Annual revenues ca. 20M EUR, +50% third parties.

~ 80 scientists (40% PhD, 60% Bachelor).


### DSM Resolve - Unique analytical capabilities

<table>
<thead>
<tr>
<th>Capability</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Molecular Imaging</strong></td>
<td>Integrate micro- &amp; spectroscopy to probe the distribution &amp; organization of polymers in (Bio) materials.</td>
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<tr>
<td><strong>Materials &amp; Chemical processing</strong></td>
<td>Create profound understanding in design &amp; upscaling by integrating off-in- or on-line monitoring strategies with chemo-metrics.</td>
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<tr>
<td><strong>Catalyst characterization</strong></td>
<td>Correlate morphology of Catalysts materials to performance, fouling &amp; reaction kinetics.</td>
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<tr>
<td><strong>Macromolecular characterization</strong></td>
<td>Relate details in molecular microstructures of poly-disperse (bio)polymers to materials properties.</td>
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<tr>
<td><strong>Small molecules profiling</strong></td>
<td>Employ state-of-the-art hyphenated separation technologies to characterize complex mixtures.</td>
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Developments in Polymer Analysis @ DSM

- Corporate program on (Bio)Macromolecular Analysis:
  - Chemical heterogeneity.
  - Very high molar masses.
  - 3D structures.
  - Quantification aspects.
  - Screening of additives.
  - Enhanced extractions, sample prep.

- Analytical technologies involved:
  - GPEC, 2DLC (off-line, on-line).
  - AF4.
  - DOSY-NMR, HR NMR.
  - HR-MS, IMS-MS, MALDI.
SEC in industrial applications - 2016

- **Gap** between academic research and industrial practice on polymer separations.

- **SEC**: one of the most used techniques for polymer characterization in industry.

- Considered as simple, but still many pitfalls.

- Real life accuracy and precision often cumbersome - how come?
SEC; accuracy and/ or precision?

- **Often**: precision more important than accuracy:
  - Trends.
  - Quality control.
  - Polymer users.

- **Accuracy**:
  - Polymer manufacturers: modelling, understanding.
  - Polymer users do not want to be too far “off”.
  - Improved accuracy plus information density by DV and LS detection - but at cost of precision.
Precision in modern SEC

1. Flow stability
   - For conventional and universal calibration. Use flow marker.
   - Not (much less) for 3SEC.
   - RI is known ‘unstable’, especially in e.g. HFIP and high temperatures.

2. Column stability
   - Mechanical and chemical.
   - Polymer versus silica.
   - Eluent type, e.g. THF worse than HFIP.
   - Standards batch to batch variations or different manufacturers.
   - Sample: molar mass level, concentration (depends on MM), dn/dc.

Precision is worst for universal calibration
Better for conventional calibration (only one detector, no accurate weighing)
Also better for Light Scattering/ 3SEC (no calibration).
Some precision numbers from our lab

1. **3SEC in THF (PS, Mw = 200 kDa)**
   - Within one run (n = 10, RSD, 1σ)
     - $M_n$: 5% - $M_w$: 2% - $M_z$: 3% - $[\eta]$: 1%.

2. **3SEC in HFIP (PA, Mw 60 kDa)**
   - Short term (5 weeks, n = 26, RSD, 1σ)
     - $M_n$: 3% - $M_w$: 3% - $M_z$: 3%
   - Long term (2 years, RSD, 1σ)
     - $M_n$: 10% - $M_w$: 10% - $M_z$: 10%

3. **HT-SEC – DV (NBS1475A, Mw = 56 kDa)**
   - Short term (1 run, n = 10, 2σ)
     - $M_n$: 10% - $M_w$: 8% - $M_z$: 11% - $[\eta]$: 4%.
   - Long term (2 years, n = 220, 2σ)
     - $M_n$: 15% - $M_w$: 10% - $M_z$: 13% - $[\eta]$: 6%

4. **HT-SEC – LS (NBS1475A, Mw = 56 kDa)**
   - Long term (2 years, n = 220, 2σ)
     - $M_n$: 12% - $M_w$: 2% - $M_z$: 10%
Base line issues affecting precision

Improvement of baseline stability on transferring high temperature SEC (solvent: TCB, T: 160 C) from RI to IR detection (broad band filter)
Improved precision via more stable detection
IR versus RI detection in HT-SEC

SPC sample *(NBS1475A, linear PE)*

**PolymerChar Infrared detection**

<table>
<thead>
<tr>
<th></th>
<th>Mn</th>
<th>Mw</th>
<th>Mz</th>
<th>Mw/Mn</th>
<th>Mz/Mw</th>
<th>IVw</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>14.0</td>
<td>56.3</td>
<td>182.3</td>
<td>4.03</td>
<td>3.24</td>
<td>1.02</td>
</tr>
<tr>
<td>SD</td>
<td>0.51</td>
<td>1.80</td>
<td>6.81</td>
<td>0.12</td>
<td>0.07</td>
<td>0.02</td>
</tr>
<tr>
<td>RSD (%)</td>
<td>4%</td>
<td>3%</td>
<td>4%</td>
<td>3%</td>
<td>2%</td>
<td>2%</td>
</tr>
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- Improvement of precision.

- Some systematic differences in $M_n$ and $M_z$ - which can (and must!) be explained.

**Viscotec Refractive Index detection**

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<tr>
<th></th>
<th>Mn</th>
<th>Mw</th>
<th>Mz</th>
<th>Mw/Mn</th>
<th>Mz/Mw</th>
<th>IVw</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>15.3</td>
<td>55.2</td>
<td>166.4</td>
<td>3.61</td>
<td>3.01</td>
<td>1.03</td>
</tr>
<tr>
<td>SD</td>
<td>0.82</td>
<td>1.91</td>
<td>7.92</td>
<td>0.13</td>
<td>0.14</td>
<td>0.03</td>
</tr>
<tr>
<td>RSD (%)</td>
<td>5%</td>
<td>3%</td>
<td>5%</td>
<td>4%</td>
<td>5%</td>
<td>3%</td>
</tr>
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Correlation study IR versus RI detection for PE

\[
\begin{align*}
\text{Mn: } \quad y &= 1.019x \\ R^2 &= 0.9654 \\
\text{Mw: } \quad y &= 1.0067x \\ R^2 &= 0.9782 \\
\text{Mz: } \quad y &= 0.899x \\ R^2 &= 0.9803 \\
\text{IVw: } \quad y &= 1.0022x \\ R^2 &= 0.9993
\end{align*}
\]
Example: multi detector approach with less emphasis on accuracy

- Polymer users perspective:
  - Precision more important than accuracy.
  - Characterization and comparison of ‘unknown’ products and formulations.

- Multi detector approach: SEC coupled to PDA-UV/VIS, RI, DV and LS provides a wealth of information from one single analysis:
  - ‘Rough’ molar mass distributions (DV/LS).
  - Information on branching/conformational differences (DV).
  - Rough impression of chemical composition (PDA-UV).
  - Presence of gels (DV) and particles (LS).
  - Information on blending (PDA-UV, RI).
**Example: multi detector approach.**

Comparison of UV and RI:
no blend of chemically different compounds.

**UV-DAD:**
- No significant impurities, i.e. no blend of chemically different compounds.
- Except one peak eluting before total exclusion area.
Example: multi detector approach..

From UV-DAD:
- Classification polymer type: polyester (1, 2).
- Detection and classification of dye (3).
- Indication of gel particles (4).
Example: multi detector approach..

\(^3\text{SEC (RI-DV-LS)}:\)
- Molar mass averages.
- Information on branching indicates highly branched structures.
- LS indicates gel particles.
Accuracy in modern SEC

- Real accuracy **way more difficult** to achieve than ‘good’ precision.

- **Most important error sources:**
  - Concentration:
    - Moisture, solvents, additives.
    - Exceeding overlap concentration.
  - $dn/dc$ (copolymers, polyelectrolytes).
  - Enthalpic effects (non-ideal SEC).
  - Pore mismatch.
  - Shear and/or slalom effects.
  - Calibration and alignment of the detectors (‘peak parameters’).
  - Data-analysis: integration, side products.
  - Scattering angle (LALS, RALS, MALS).
Revisiting calibration of SEC in HFIP

- Our case:
  - slightly wrong dn/dc ratio of PMMA to Nylon.
  - Mw value of PMMA standard appeared not correct.

- New broad PMMA standards (NIST), correct dn/dc (ratio): correct values for Nylons calculated via universal calibration.

- Work still in progress..
Accuracy: pore mismatch

Obvious example: (wrong) combination of $10^4$ and 100 Å column

More resolution in the low molar mass region leads to distortion of peak shape, also effecting accurate MMD.
Accuracy: pore mismatch

Less obvious example: linear PFG columns (1000 + 100 Å)

Pore mismatch: still often overlooked but affects accuracy! Use good quality, linear columns!

Non-perfect linearity, only observed from accurate ‘universal’ calibration curves deduced from ³SEC or DV/RI with many points.
Accuracy: end of integration, $M_n$ issue

- Concentration, signal to noise.
  > Influences $M_n$ due to invisibility of lowest molar mass parts.

- Concentration signal is a function of molar mass up to $M \approx 2000$.
  > Effect on accuracy $M_n$.

- Dealing with different detectors.
  > Comparing $M_n$ from universal calibration and Goldwasser method (only using viscosity signal and total sample amount).

Experience: use DV signal for determining integration end.

- Which components to include?
  > Depending on the polymerization model. E.g.: for polycondensations (low molar mass) cyclics not included in (most) models!
Accuracy: practice compared to theory - Flory plots

High quality SEC: excellent agreement (Flory) theory and SEC practice!

Red: calculated MMD. Blue: Flory fit for a linear polyamide.

Green: residuals, end of integration determined by RI = 0 (NOT correcting for mass (peak area) taken into account).
Quantitative branching information still challenging.

- Spectroscopy provides averages and often lacks sensitivity or resolution.
- Rheology relies on models.
- IMS-MS still in its infancy.
- SEC relatively strong for both LCB and SCB, quantification needs attention.
Recent progress on SCB quantification

HT-SEC coupled to IR detection for SCB quantification in polyolefins

- Quantification of SCB: via ratio of the CH3 and CH2 band signals.
- Calibration with standards with known amounts of CH3/1000 C.
- CH3/CH2 ratio plotted as function of CH3/1000 C.
- Correction for CH3 end groups.
SCB quantification via SEC-IR

- For non-C3 branches up to 60 CH₃/1000C one (linear) calibration line applicable, (+/- 2.7 CH₃/1000C), irrespective of co-monomer type.

- Calibration lines up to 100 wt% co-monomer (C3 and C4) show quadratic relation. (C3; +/- 9 CH₃/1000C (valid 50 - 335 CH₃/1000C).

SCB quantification via SEC-IR

- Calibration from copolymers or from blends leads to identical results. 
- Bandwidth of the detector filters critically determine shape of calibration curve.
- Simulated calibrations excellently correspond to practice. Detector now very well understood!

Despite very good analytical performance:

We need a better LOD!
(down to 0.1 CH₃/1000C)
Quantification of LCB

- LCB can be detected relatively sensitive via SEC-DV.

- Accurate quantification of LCB not trivial.

- Zimm-Stockmayer theory related to $R_g$ rather than $R_h$ and holds for theta conditions.

- Correlation between $R_g$ and $R_h$: draining factor $\epsilon$, not exactly known.

$$g' = g^\epsilon$$
SEC for very high molar mass polymers

- “Late co-elution”. Effect increases with decreasing $d_p$ and increasing flow rate.
- Effect can be somewhat suppressed but not completely prevented.
Slalom effects, coil-stretch transition

High molar mass molecules need to reorganize and slalom through the beads. Highest M will elute last!!!

Figure 6. (A) Sphere packing (left) and corresponding time sequence of DNA conformations (right) for $De = 0.8$. Flow is from bottom to top. (B) Overlaid fluorescence and optical images showing DNA between particles at 0.0 s (dotted box in (A) indicates region displayed in (B)).
Slalom chromatography

Chromatograms of PS standards in slalom mode.
Acquity UPLC BEH C18 Column 100 × 2.1 mm I.D; 1.7-μm particles.
Flow rate 0.7 mL/min; mobile phase THF; ambient temperature.

Data from E.V. Uliyanchenko, PhD thesis, Chapter 4.
Alternative: AF4?

Molecular characterization of UHMW polymers still needs further development.
Fast SEC - APC

Yes:

- Much faster results.
- Higher resolution, especially in low molar mass range.
- Less waste.
- Flexibility in solvent composition (rigidity of column packing).

But also a few catches..
APC: flow rate affects elution volume

- Increasing elution volume on increasing flow rate, for higher masses (from $10^5$ kDa).

- Slalom effects?

- P affecting coil density?

Effect of flow rate (0.2 - mL/min) on elution volume. Solvent: NMP.
APC: varying molar mass compared to SEC

\[ M_p \] values for 8 saturated polyester samples in NMP (PS calibration).

\[ M_p \] values for 20 non-functional acrylate samples in NMP (PS calibration).
APC: flow rate affects elution volume

- Sample dependent results indicate non-SEC effects. No other column packing types (yet) available to help prevent this. Solvent triangle!

- Changing molar masses values requires effort for implementation.

- Observation: column clogging for various semi-crystalline polyesters. Not observed in SEC.

- LS detector available nowadays but DV not (yet).

- Use of high flow rates needs further attention!

APC is interesting for its speed and flexibility but needs further attention!
Chemical composition separation by GPEC

- Separation of various polyamide types by Gradient Polymer Elution Chromatography (GPEC).
- Separation based on chemical composition plus molar mass.

Increasing retention (x-axis) from increasingly non-polar polyamides.
Chemical composition separation by GPEC

- Next step: 2D-LC, e.g. SEC-GPEC OR GPEC-SEC:
- More details, (small) differences.
- Quantification of CCD?!
2D-LC for polymers: on-line or off-line?

**On-line**

**Advantages**
- No laborious sample (fraction) prep.
- (Coupled to the above): suited for large series and standardized applications.
- ‘Sexy’..

**Disadvantages**
- Interfacing still cumbersome due to e.g. solvent mismatch issues *(strength, viscosity, miscibility)*.
- Time-consuming setting-up per application.
- No free choice of order of dimensions.
- Second dimension resolution limited. *(SEC..).*

**Off-line**

**Advantages**
- No ‘complex’ interfacing.
- For incidental applications and freedom to choose separation order.
- Maximum separation power in both dimensions.
- Fractions also available for e.g. NMR and titrations.

**Disadvantages**
- Relatively laborious (sample prep).
- Critical to pollution (eluent!).
- Sometimes unexpected effects (adsorption at tubing etc.).
2D-LC for polymers: in practice

- Despite developments since ~15 years: use of on-line 2DLC for polymers seems rare.

- Quantification in 2DLC seems completely neglected in research. E.g. accuracy, precision of 2nd dimension SEC?
Our practice: working on both on-line and off-line coupling

- **On-line 2DLC**
  - Striving for a few ‘standardized’ systems.
  - Collaboration with Universities to speed-up implementation. Projects on e.g. fast method optimization.

- **Off-line 2DLC**
  - Streamlining fractionations.
  - Developing sample prep. Strategies for e.g. HFIP-KTFA systems.
Example on-line 2D chromatography

On-line 2D-LC separation (RPLC×HILIC) of oligomers with different end groups. Structured Chromatograms.

First results LC×SEC of polymer blending. Little SEC resolution.
Example off-line 2D chromatography

- Issues on setting-up SEC fractionation from HFIP/KTFA:
  - Adsorption to Teflon tubing.
  - Preventing contaminations.
  - Removal of salt by SPE:
    - Adsorption of KTFA to C18: optimization of desorption conditions.
    - Drying and re-dissolution procedure on the C18 cartridge.
  - Now ready for further work. Already new details visible on polymers.

Low polydispersity fractions from SEC.

First results SEC-GPEC for a polyamide.
Conclusions

- Value of modern SEC can hardly be overestimated but..

- Establishing accurate and precise systems is still not trivial (for many users).

- Need for better, more precise and sensitive branching characterization.

- Need for better methods for very high molar masses especially at high temperatures.

- Fast SEC (APC): need for other column packings; beware of too high speeds.

- 2D LC for polymers is still in its infancy: quantification!
Acknowledgements

Tiny Frijns
Sandra van der Flier
Artur Henke
Sander Kok
Joep Vanderfeesten