GPC/SEC Troubleshooting Guide

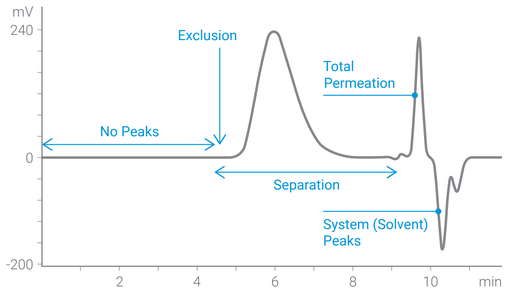
Your guide to solving common problems and staying productive

Agilent InfinityLab

Places to Start

Solvents

- Always choose HPLC-grade solvents and filter through 0.02–0.45 µm filters
- Use stabilized solvent when appropriate (e.g., THF stabilized with butyl hydroxylated toluene (BHT) to extend column lifetimes)
- Use solvent additives as recommended to suppress any interaction between the sample and the columns



Typical regions of a GPC chromatogram

Day to Day

- Don't shut the system down with the columns connected; reduce the flow rate to 0.1 mL/min (recycle if required)
- If removing the columns for any length of time, make sure they are stored in the recommended solvent and that the end caps are correctly fitted
- If using buffers, flush the column into pure solvent when analysis is complete
- Make sure that any solvent change is to (or via) a miscible solvent; flush with at least three column volumes or preferably overnight

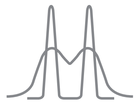
Sample Preparation

- Dissolution time and temperature will depend on molecular weight and crystallinity of polymer; stirring may aid dissolution but avoid sample degradation
- Always use an aliquot of the mobile phase to prepare the solution
- Filter samples to remove any insoluble material (0.5–1.0 µm filters)
- Remember: sample concentration is critical if using light scattering or viscometry detection; ensure there is no solvent evaporation from the vial prior to analysis

Peak Tailing

Possible Cause	Solution
Excessive dead volumes	Minimize tubing length Tighten injection seal Check connector fittings
Column degradation	Replace or repair column
Column interaction	Use mobile phase additives
Shear degradation	Replace standard solutions every two weeks Modify dissolution process (no excessive shaking)

Peak Broadening

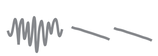


Possible Cause	Solution
Large dead volume	Minimize tubing/check fittings
Eluent too viscous	Use column oven
Detector cell too large	If possible, use smaller cell volume

Coeluting Peaks

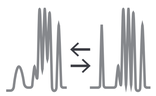
Possible Cause	Solution
Sample is copolymer or blend	Select set of columns with wider resolving range If peaks cannot be separated, always analyse sample as though single peak

Baseline Drift/Noise



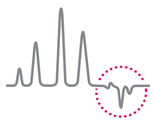
Possible Cause	Solution
Column/detector contamination	Flush column/detector to waste Clean eluent Use better quality solvents
Bubbles in detector	Degas solvent
Temperature variations	Use column heater/insulate tubing

Resolution



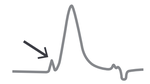
Possible Cause	Solution
Analyzing polymers or monomers?	Choose correct column pore size
If main peak is above the resolving range of the columns, sample is "excluded" from columns	If main polymer peak is main focus, then increase column pore size to cover molecular weight range of sample

Ghost Peaks



Possible Cause	Solution
Peaks carried over from previous injection	Let previous sample fully elute before next injection
If absorption occurs, some material may elute after total permeation limit	Either add buffer to mobile phase or switch to a different solvent

Partial Peak Exclusion

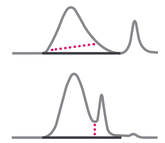


Possible Cause	Solution
Dead space of separation around half of total elution volume	Add columns with higher molecular weight-resolving range
Peaks eluting close to this volume may be partially excluded	Possibly increase to 5–10 µm particle size
Look for sharp peaks at the front of your chromatograms	Only reduce number of columns if faster run times are important and lower resolution is acceptable

Increased Retention Time

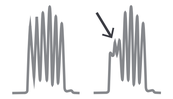
Possible Cause	Solution
Flow rate reduction	Check for bubbles in pump head Degas solvent
Interaction with packing	Use modifiers/additives
Sample adsorption	Change eluent polarity

Incorrect Molecular Weights



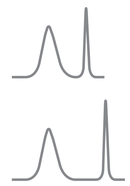
Possible Cause	Solution
Improper selection of baseline and integration limits	Analyze whole peak for true reflection of sample Select integration limits down to baseline on either side of peak (solid black line is correct) Excluding components of peak will give incomplete MWD and incorrect molecular weight values

Peak Splitting



Possible Cause	Solution
Sample loading too large	Reduce loading/loop size
Blocked/partially blocked frit	Replace frit; use 2 µm inline filter to stop clogging
Void in column	Replace column
Partially blocked injection valve	Replace rotor seal

Molecular Weight Variations



Possible Cause	Solution
Pump drift; column aging; new capillaries; reswaged fittings; new column connections	Mark end of run with small molecule such as toluene, BHT, acetone, or ethylene glycol Narrow peak marker (internal standard) to measure column efficiency and identify degradation, tailing, and retention shifts not obvious with broad sample peaks Recalibrate columns regularly Check pump flow rate is consistent Check any fittings for leaks If symptoms continue, replace columns

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