

ANALYSIS OF PLGA MOLECULAR WEIGHT AND STRUCTURE BY THE LATEST ADVANCED MULTI-DETECTOR GPC SYSTEMS

Introduction

- Triple Detection GPC/SEC (TD-GPC) using refractive index (RI), viscometer and light scattering (LS) detectors has now been in routine use for over 10 years for many applications.
- However, the use of light scattering has been limited for some applications due to instrument's sensitivity.
- One such example is polylactide (PLA) and poly(lactic-co-glycolic acid) (PLGA). Many samples of this type are well soluble in tetrahydrofuran (THF)
- PLA, PLGA and their copolymers are biocompatible, biodegradable and used in a number of medical applications such as for implants, stents, sutures and drug delivery systems.
- As the monomers can be derived from renewable sources, PLGA is considered to be a "green" material. PLA also finds use in 3D printing systems due to its relatively low glass transition temperature.

The challenge

- The Rayleigh equation shows that the scattered light intensity (R_0) is proportional to molecular mass (M_w), concentration (c) and squared refractive index increment $(dn/dc)^2$.

$$R_0 \propto M_w \cdot c \cdot \left(\frac{dn}{dc}\right)^2$$

- The refractive index increment (dn/dc) for PLA/PLGA in THF is low at around 0.05 mL/g
- At the same concentration and molecular mass as a polystyrene sample in THF with a dn/dc of 0.185 mL/g, the PLA / PLGA sample will show a response of just about 7 % on the light scattering detector.
- Analysis of this low molecular weight and low dn/dc sample without increasing concentrations to column overload point pushes the sensitivity boundaries of all previous light scattering detectors.

The solution

- This poster presents data run on Malvern Instruments' OMNISEC SYSTEM for PLA and PLGA in THF.
- The light scattering detector in OMNISEC shows a great increase in sensitivity compared to other similar devices.
- This is key for applications like PLGA with low dn/dc values for the sample/solvent combination. The derived data also includes valuable structural information on the samples.

Triple Detection

- Combining light scattering, concentration and viscometer detectors, known as triple detection GPC/SEC, delivers more information than individual detectors.
- The concentration detector, typically a differential refractive index detector, records the concentration profile of the sample eluting from the column.
- The LALS/RALS light scattering detector measures molecular weight, having both the sensitivity for small molecules as well as the ability to measure large molecules.
- The viscometer measures intrinsic viscosity, which shows the density of the molecules and changes in structure.
- Combining the detector signals also provides hydrodynamic radius, Mark-Houwink plots (intrinsic viscosity vs. molecular weight) and branching analysis.

Methods and Materials

- Samples were separated on an OMNISEC GPC/SEC system, with THF used as solvent for the samples as well as the mobile phase.
- Two Malvern Instruments' LT5000L columns were used for separation.
- Sample solutions were prepared to concentrations of 1 to 5 mg/mL, injection volume: 100 μ L.
- The autosampler, columns and detectors were held at 30 °C.

Results

Chromatogram

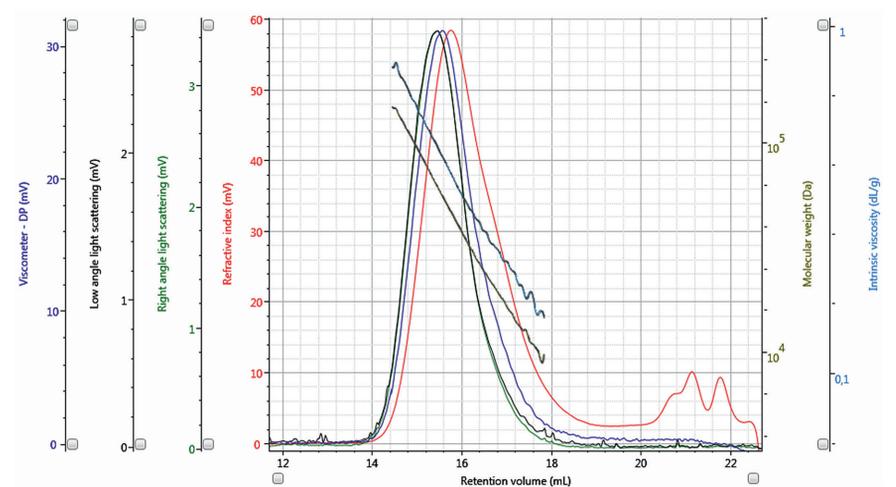


Figure 1: Chromatogram and derived data of PLGA 50:50, $M_w = 44628$ g/mol, $M_n = 26727$ g/mol, 2.132 mg/mL.

- As can be seen in Figure 1, all detectors in the OMNISEC system show excellent signal to noise ratios.

Molecular structure

- A plot of intrinsic viscosity against molecular weight, Figure 2, shows clearly different positions for the different compositions of PLGA copolymers, with the two samples of 50:50 copolymer overlaying confirming the position is composition related not molecular weight related.
- This can also be used to monitor compositional changes e.g. during a degradation study or in quality control applications.

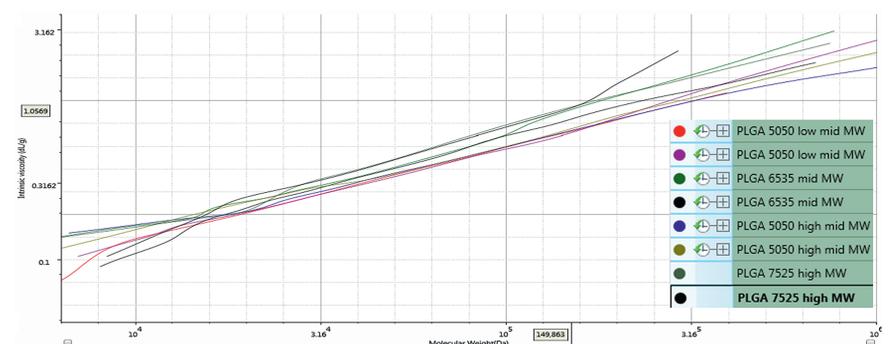


Figure 2: A Mark-Houwink plot reveals structural and compositional differences between the various PLGA samples

Repeatability

- 10 repeat injections of 100 μ L were performed on a PLGA sample with 50 % lactic acid content at a concentration of 2.132 mg/mL. Table 1 shows the measured parameters together with their respective relative standard deviation, proving the excellent repeatability of the data obtained.

Parameter	Average value	Unit	RSD / %
M_n	26.102	g/mol	2.32
M_w	44.722	g/mol	0.37
M_z	67.009	g/mol	1.22
$[\eta]_w$	0.36	dL/g	1.37
$R_{h,w}$	6.07	nm	0.50
Recovery	100	percent	0.53

Table 1: Measured parameters for 10 repeat injections of a PLGA sample with 50% lactic acid content.

Conclusions

- TD-GPC delivers far more information about a sample than conventional GPC with individual detectors
- The high sensitivity of the OMNISEC system compared to all previous devices allows measurement of low dn/dc and low molecular weight samples such as PLA and PLGA at normal concentrations and with excellent repeatability.
- The composition of the PLGA co-polymers can be tracked or identified via the clear structural differences shown in the Mark-Houwink plots.