

Particle Characterisation

Characterising thermally induced gelation in methylcellulose formulations using dynamic light scattering

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Thermoresponsive polymers such as methylcellulose undergo pronounced, reversible sol–gel transitions that are central to their performance in pharmaceutical, biomedical, food, and personal care formulations. Accurately determining the onset and progression of gelation can remain challenging, particularly when early molecular or microstructural changes are of interest. Conventional bulk methods provide valuable information on thermal transitions, optical changes, and mechanical behaviour, but may not always fully resolve the subtle changes that precede clearly detectable macroscopic network formation.

This article explains how dynamic light scattering (DLS), together with measurements of scattered light intensity and transmittance, can track methylcellulose gelation from early molecular changes to macroscopic gel formation. Temperature-dependent measurements reveal clear stages of gelation, from early changes in molecular mobility to network formation and visible clouding. The impact of ionic strength on gelation temperature is measured, demonstrating the value of dynamic light scattering for formulation screening and smart material design.

“Dynamic light scattering captures the full gelation pathway of methylcellulose - from molecular motion to macroscopic gel formation.”



Figure 1: Litesizer DLS 501 particle size analyser employing dynamic light scattering (DLS).

Introduction

Thermoresponsive polymers are an increasingly important class of smart materials, distinguished by their ability to reversibly change physical properties in response to temperature. Among these materials, methylcellulose holds a unique position due to its unusual sol–gel transition behaviour: It is readily soluble in cold water yet undergoes gelation when heated. This inverse thermal response enables precise, temperature-triggered control of viscosity, structure, and mechanical strength, making methylcellulose highly attractive for applications requiring predictable and reversible material behaviour.

Methylcellulose is widely used across diverse industries, including pharmaceuticals, biomedical engineering, food technology, cosmetics, and construction materials. In pharmaceutical and biomedical contexts, its ability to gel near physiological temperatures enables applications such as controlled drug release, injectable hydrogels, and bioinks for tissue engineering. In the food industry, heat-induced gelation provides texture and stability in processed and plant-based products, while in personal-care formulations, it functions as a thickener and film-forming agent. Across all these applications, performance is directly linked to the temperature at which gelation begins and how the underlying polymer network develops.

Despite its broad use, accurately identifying the onset and progression of methylcellulose gelation remains challenging. Established characterisation techniques such as rheology, differential scanning calorimetry, turbidimetry, and simple tube-inversion tests provide valuable information on thermal transitions, optical changes, and bulk mechanical behaviour. However, depending on the method and evaluation criteria used,

they may be less sensitive to the subtle molecular associations and microstructural changes that occur before a clearly detectable macroscopic gel network has developed.

Light scattering methods, especially dynamic light scattering (DLS), provide an additional way to study these processes. By measuring temperature driven changes in scattered light, DLS can detect variations in molecular movement and particle association at nanometre scales. Dynamic light scattering enables access to the diffusion coefficient, scattered light intensity, and transmittance within a single measurement, providing a comprehensive view of thermogelation from dispersed polymer chains to network formation and macroscopic turbidity.

In this study, the thermoresponsive behaviour of methylcellulose was investigated using DLS measurements performed over a controlled temperature range. By monitoring the diffusion coefficient, scattered-light intensity, and transmittance at the same time, gelation can be divided into distinct structural stages. The effect of ionic strength on the gelation temperature was also investigated, showing how formulation conditions relevant to physiological and industrial settings influence polymer association and network formation. Together, these findings demonstrate that dynamic light scattering is a sensitive, non-invasive technique for formulation screening, smart-material development, and process optimisation.

Limitations of conventional gelation characterisation

Gelation of methylcellulose is traditionally assessed using methods such as:

- Bulk rheology
- Differential scanning calorimetry (DSC)
- Turbidimetry
- Viscometry or tube inversion tests

These methods provide valuable information on macroscopic properties, including mechanical behaviour, thermal transitions, optical changes, and flow characteristics. However, depending on the technique and evaluation criteria used, they may be less sensitive to the early molecular associations and microstructural changes that occur before substantial network formation becomes evident. These early-stage changes can play

an important role in determining formulation stability, processability, and reproducibility.

As a result, formulation screening based solely on bulk techniques may be time-consuming and may overlook subtle but relevant changes during the initial stages of gelation.

Dynamic light scattering as a comprehensive tool for studying thermogelation

DLS makes it possible to observe the earliest structural changes by monitoring the temperature-driven motion of molecules and aggregates in solution. In addition to standard particle size information, modern light scattering instruments can measure several parameters at the same time:

- **Diffusion coefficient**, which reflects molecular mobility and the onset of aggregation
- **Mean scattered light intensity**, which indicates increasing structural heterogeneity as networks begin to form
- **Transmittance**, which captures macroscopic clouding and bulk gel formation.

Together, these measurements provide a continuous view of thermoresponsive transitions across different structural levels, from early nanoscale association to fully developed macroscopic gels. This study shows how this approach was applied to methylcellulose using the Litesizer DLS 501, providing detailed insight into gelation behaviour and the effects of formulation conditions.

Methodology

Commercial methylcellulose powder was first characterised by dynamic image analysis using the Litesizer DIA 700 to establish its primary particle size distribution before dissolution.

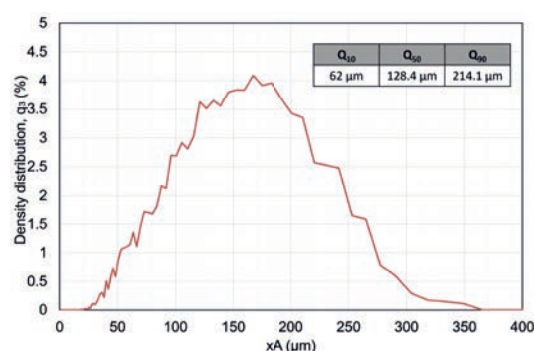


Figure 2: Particle size distribution of methylcellulose powder measured by dynamic image analysis, showing $Q_{10} = 62.0 \mu\text{m}$, $Q_{50} = 128.4 \mu\text{m}$, and $Q_{90} = 214.1 \mu\text{m}$ [HB1.1].

For thermogelation studies, methylcellulose was dissolved at 1% (m/V) in two solvents:

- Ultrapure water
- 0.9% (m/V) NaCl solution

The saline solution represents physiological ionic strength and allows assessment of formulation effects relevant to biomedical applications. All solvents were pre filtered ($0.022 \mu\text{m}$) to eliminate dust and particulate contamination.

The methylcellulose powder was slowly introduced under continuous stirring and diluted to a final concentration of 1% (m/V) to achieve homogeneous wetting and dissolution. All samples were allowed to equilibrate completely before particle size measurements were performed.

Temperature series DLS measurements

Temperature dependent measurements were performed using a Litesizer DLS 501 with quartz cuvettes. Samples were heated from 30°C to 70°C in 2°C increments, with a one minute equilibration at each step, followed by 100 runs of 30 s.

Although particle size analysis was selected as the measurement mode, the primary focus was placed on the diffusion coefficient, mean scattered light intensity, and transmittance.

These parameters provide higher sensitivity to gelation phenomena than particle size alone once the system departs from ideal dilute conditions.

Interpretation of the diffusion coefficient

In dilute solutions below the gelation temperature, the diffusion coefficient, derived from the temporal fluctuations of scattered light, can be related to hydrodynamic size using the Stokes–Einstein equation and reflects particle movement. The polymer chains are still dispersed or loosely associated and freely undergo Brownian motion.

As gelation progresses, the interpretation of the diffusion coefficient becomes increasingly complex. During this stage, methylcellulose undergoes structural changes that promote aggregation, network development, and eventually dynamic arrest. Under these conditions, the assumptions of the Stokes–Einstein equation are no longer valid:

- The system no longer behaves as a simple Newtonian fluid
- A single, well defined viscosity can no longer be assigned
- Particle motion is progressively limited by the growing microstructure, rather than determined solely by hydrodynamic effects.

Temperature dependence of the diffusion coefficient

The evolution of the diffusion coefficient reveals three distinct regimes during methylcellulose thermogelation, as shown in Figure 3:

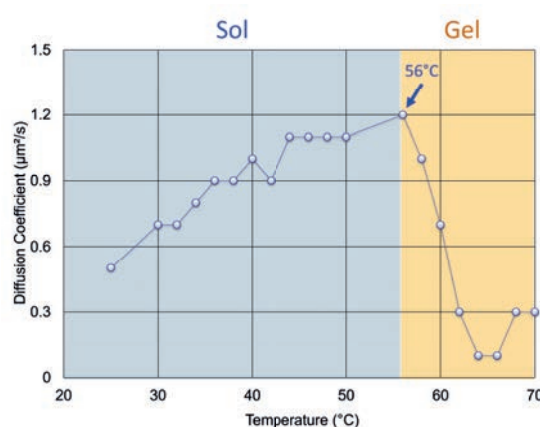


Figure 3: Diffusion coefficient of methylcellulose as a function of temperature, showing sol, transitional, and gelation regimes.

1. Sol state ($\approx 25\text{--}40^\circ\text{C}$)

The diffusion coefficient increases gradually, reflecting enhanced thermal motion of polymer coils in solution.

2. Transitional regime ($\approx 44\text{--}50^\circ\text{C}$)

A plateau in diffusion indicates early chain association and reduced mobility due to emerging interchain interactions.

3. Gelation onset ($\approx 56^\circ\text{C}$)

A sharp collapse of the diffusion coefficient marks the formation of a percolating polymer network and the onset of dynamic arrest.

This collapse provides a precise and early indicator of gelation that precedes macroscopic changes detectable by bulk methods.

Mean scattered light intensity

Mean scattered light intensity increases as microstructural heterogeneity grows.

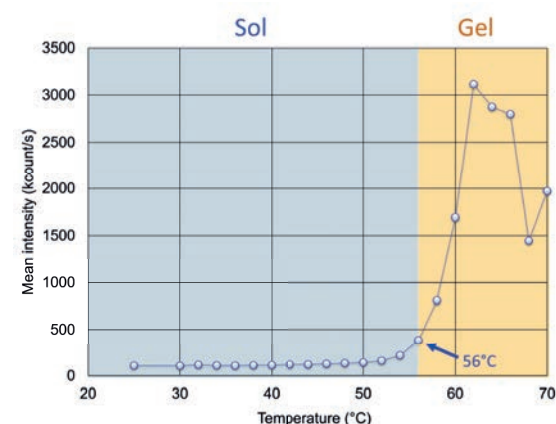


Figure 4: Mean scattered light intensity versus temperature, showing a gradual increase near gelation and a sharp rise during network formation.

At temperatures around 50°C to 56°C , intensity begins to rise, signalling the formation of larger associative structures. Above $\approx 56^\circ\text{C}$, intensity increases steeply and becomes more variable, consistent with a strongly scattering gel network (Figure 4).

Transmittance and macroscopic gelation

Transmittance measurements provide a complementary bulk perspective.

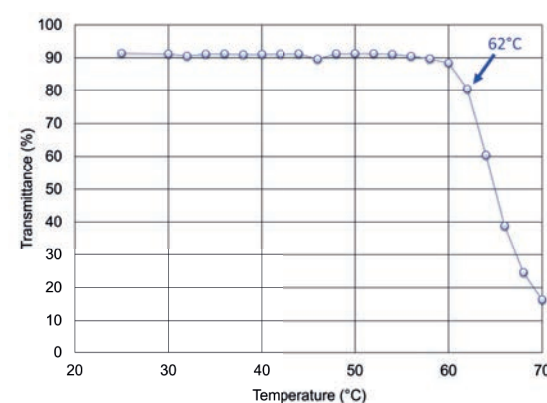


Figure 5: Optical transmittance of methylcellulose as a function of temperature.

Unlike diffusion coefficient and mean intensity, transmittance remains high until $\approx 60^\circ\text{C}$ to 62°C , when a sharp drop occurs. This delayed response reflects the fact that transmittance only detects gelation once sufficient refractive index contrast and turbidity have developed.

Together, the three parameters map gelation across length scales:

- Diffusion coefficient (earliest, nanoscale signal)
- Mean intensity (intermediate, microstructural development)
- Transmittance (latest, macroscopic gel formation)

Effect of ionic strength on gelation

Introducing 0.9% NaCl significantly shifts gelation to lower temperatures.

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Across all parameters, gelation occurs approximately 4°C earlier in saline solution. Ionic strength promotes hydrophobic association by screening electrostatic interactions, reducing the energy required for network formation. This effect is particularly relevant for biomedical and physiological applications, where methylcellulose is rarely used under pure water conditions.

Discussion and analysis

The results show that thermogelation of methylcellulose is a gradual, multi-stage process rather than a single abrupt transition. Early heating induces subtle changes in molecular mobility as polymer chains begin to associate. This is followed by the formation of interconnected microstructures and, ultimately, a continuous network responsible for macroscopic gelation and turbidity. Capturing these sequential stages requires techniques that are sensitive to structural changes long before bulk gel formation becomes apparent.

Dynamic light scattering is particularly effective in this regard, as it detects changes in particle motion and structural organisation that are often missed by conventional bulk methods. Simultaneous monitoring of the diffusion coefficient, scattered-light intensity, and transmittance enables earlier identification of gelation onset and facilitates comparison between formulations, revealing how factors such as solvent composition, ionic strength, and additives influence network formation.

Importantly, the diffusion coefficient remains informative even when classical particle-size interpretation is no longer valid. As gelation progresses, it reflects increasing constraints on molecular motion rather than true free diffusion, making it a sensitive indicator of structural evolution and material dynamics. At later, fully non-ergodic stages, light-scattering data are best interpreted qualitatively; nevertheless, the combined analysis remains highly valuable for

comparing formulations, identifying gelation trends, and defining processing windows relevant to smart-material development and industrial applications.

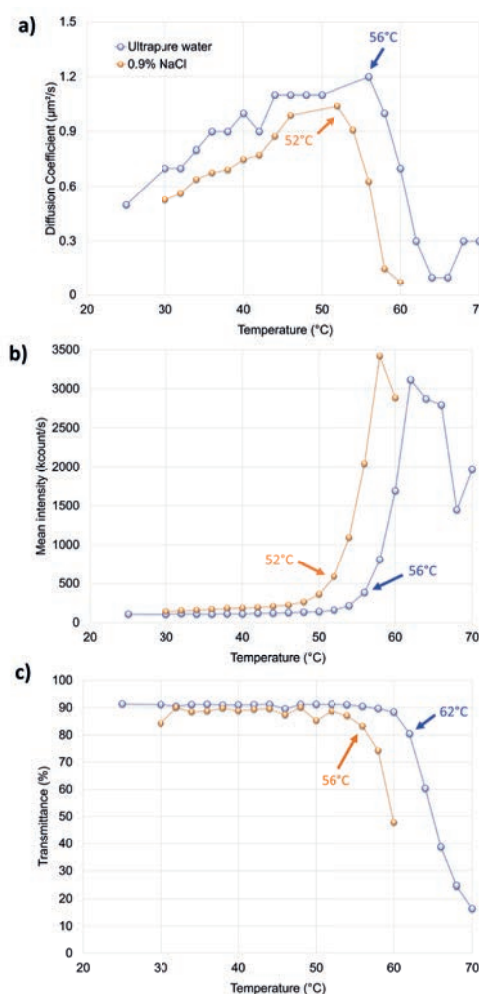


Figure 6: Comparison of methylcellulose gelation in ultrapure water and 0.9% NaCl using diffusion coefficient (a), mean intensity (b), and transmittance (c).

Conclusion

Dynamic light scattering, as implemented using the Litesizer DLS series, provides a powerful and non-invasive approach for characterising thermoresponsive materials such as methylcellulose. From a single DLS temperature-dependent measurement, parameters including the diffusion coefficient, scattered-light intensity, and transmittance can be extracted, enabling comprehensive analysis of the gelation process. This approach enables earlier detection of gelation than conventional methods, examines the effects of formulation conditions such as ionic strength, and delivers useful insight for material design, process optimisation, and quality control. By extending DLS beyond particle size to include dynamic and structural information, formulators gain a clearer understanding of thermoresponsive behaviour that is essential for modern pharmaceutical, biomedical, and food applications.

Reference

1. Thirumala, S.; Gimble, J. M.; Devireddy, R. V. Methylcellulose Based Thermally Reversible Hydrogel System for Tissue Engineering Applications. *Cells*, 2013, 3(2), 460–475. <https://doi.org/10.3390/cells2030460>
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