What does solubility mean in CE of macromolecules, and in macromolecular characterisation in general? How can CE help?

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Gold statement
- Learn about the limitations of common visual observation to assess solubility
- Discover that dissolution kinetics is full of surprises for macromolecules, but can be monitored using CE
- Learn that full dissolution may not be obtained without some chemical degradation, e.g., for chitosan

Introduction
The concept of solubility is often used in a very binary fashion in an analytical chemistry laboratory: a transparent liquid means solubility, and turbidity means insolubility. In the case of macromolecules, there are a lot more possibilities and different definitions of solubility. Depending whether one looks at functionalisation of macromolecules, spectroscopy, CE or HPLC separation or filtration for example, then one will rely on different definitions of solubility.

Body
In a strict definition of solubility, all monomer units (or base pairs, or amino acids, etc.) are in contact with the solvent. NMR spectroscopy can measure this solubility: we have shown that while starch [1], chitosan [2] or poly(acrylic acid) [3] produce transparent liquids, analysis of these suspensions by NMR determines the solubility to be incomplete. This definition of solubility does not only apply to NMR spectroscopy, it is also relevant for the functionalisation of macromolecules, e.g., drug binding to poly(acrylic acid).
Full solubility is not required to separate macromolecules using CE. While solution-state NMR spectroscopy allows to monitor but also quantify solubility in the stricter sense [1], CE allows for a quicker and easier online monitoring of dissolution as we showed in the case of chitosan [2] or poly(acrylic acid) [3].
The most common solvent for chitosan, aqueous acetic acid, may not allow quantitative dissolution, while its most “powerful” solvent, aqueous HCl, may allow quantitative dissolution but only at the expense of chemical degradation [2]. The kinetics of dissolution is not simply dependent on molecular weight: while starch has been seen to dissolve in a few minutes despite its large molecular weight, oligomers of acrylic acid can take several hours [3]!

Conclusion
A lot is still unknown in terms of solubility of macromolecules. This important step in sample preparation may be too often assumed to be properly dealt with by simple visual observation. Easy and accurate monitoring of dissolution with capillary electrophoresis yielded in-depth and surprising information for synthetic polymers and polysaccharides.

References
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